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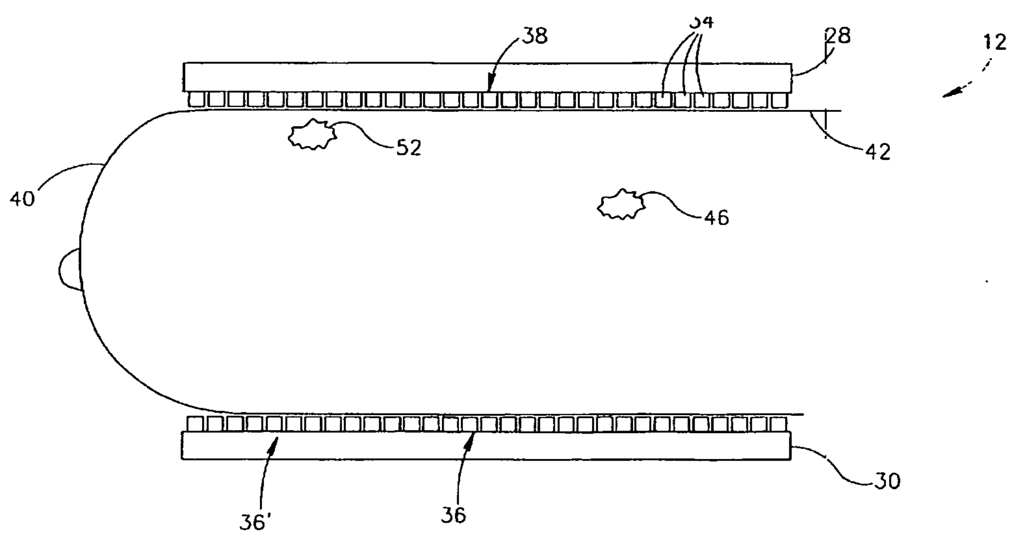
(54) Title: LOCALIZATION OF ANOMALIES IN TISSUE AND GUIDANCE OF INVASIVE TOOLS BASED ON IMPEDANCE IMAGING



(57) Abstract: Apparatus for impedance imaging of a region within a subject. The apparatus includes a plurality of electrodes adapted to, substantially concurrently, apply electrical signals having a common frequency and different phases to the subject and a plurality of sensing elements adapted to sense electrical signals from a surface of the region, responsive to signals applied from the electrodes.

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LOCALIZATION OF ANOMALIES IN TISSUE AND GUIDANCE OF INVASIVE TOOLS BASED ON IMPEDANCE IMAGING

FIELD OF THE INVENTION

The present invention relates to systems for tissue characterization based on impedance measurements, and in particular to systems for determining the locations of anomalies based on impedance measurements.

BACKGROUND OF THE INVENTION

Variations in electrical impedance of the human tissue may be indicative of tumors, lesions and other anomalies. For example, US patents 4,291,708 to Frei, and 4,458,694, and the article, "Breast Cancer Screening by Impedance Measurements," by G. Piperno et al., Frontiers Med. Biol. Eng., Vol. 2 pp. 111-117, the disclosures of which are incorporated herein by reference, describe systems for determining the impedance between a point on the surface of the skin and some reference point on the body of the patient. With the use of a multi-element probe, a two-dimensional impedance map of an organ such as a breast can be generated. The impedance map, describing variations in impedance along the tissue of the organ, can be used for the detection of tumors and especially malignant tumors.

An exemplary system for tissue characterization includes a multi-element probe which is pressed against the skin of a patient. The elements of the multi-element probe are kept at a ground voltage and an electrification signal is applied at some point on the patient. The elements of the multi-element probe serve as sensors which measure the current incident on the sensors and accordingly determine a measure of the impedance of the tissue beneath each element of the probe. Using the impedance values determined by the elements, a two-dimensional impedance map is generated, which map is used to detect abnormal tissue.

It is understood, however, that the system indicates the locations of abnormal tissue as a function of the locations on the skin, and gives little indication of the depth of the abnormal tissue beneath the skin. In addition, the ability to find a tumor of abnormal tissue decreases with the distance of the tumor from the surface to which the probe is pressed.

U.S. patents 4,617,939 and 4,539,640 describe three-dimensional mapping of the tissue impedance of the body. These patents describe measuring the impedance on a plurality of surfaces surrounding an organ and producing a three-dimensional map based on Poison's equation.

However, in many organs it is not feasible to place a sufficient number of probes on surfaces of the organ to receive a satisfactory impedance image. In addition, in some cases it is

desired that the point from which the electrification signal is applied be as close as possible to the examined organ and/or that the signal be applied along a large surface. Furthermore, in some cases the image is required during a surgical procedure, especially during minimal invasive procedures, such as biopsy taking using a biopsy needle. In such cases, a surgeon performing the procedure needs to have access to the surface of the organ.

Even when there are sufficient vacant surfaces on the organ, three-dimensional mapping is cumbersome and requires complex algorithms in order to solve Poison's equation. These complex algorithms introduce errors into the measurements and/or magnify measurement errors. In addition, when the organ includes a plurality of anomalies, separation between the different anomalies becomes very difficult, since all the anomalies influence the measurements on all the surfaces. The resolution of such imaging is not sufficient for identification of small anomalies of the order of less than a centimeter.

U.S. patent 5,353,802 to Ollmar, the disclosure of which is incorporated herein by reference, describes a device for depth selective detection and characterization of surface phenomena based on impedance measurements. The device includes an electrode for applying electrical signals, an electrode for measuring signals and a control electrode for controlling the depth of the applied signals.

SUMMARY OF THE INVENTION

An aspect of some embodiments of the present invention provides methods and apparatus for determining the depth of an anomaly within an organ of a patient, relative to a probe placed on a surface of the organ. The depth is determined using signals detected by the probe on the surface.

An aspect of some embodiments of the present invention provides methods for detecting anomalies which are deep within an organ, i.e., far from a probe of sensors used to detect the anomaly, which anomalies are not detectable using methods known in the art.

An aspect of some embodiments of the present invention provides a method for determining the depth of an anomaly within an organ, which method does not depend on the shape of the anomaly.

An aspect of some embodiments of the present invention provides improved methods for directing an invasive tool, such as a biopsy needle, toward an anomaly.

An aspect of some embodiments of the present invention provides improved methods for determining contact between an invasive tool and an anomaly.

An aspect of some embodiments of the present invention relates to applying electrifying signals for impedance imaging of a body part at specific points relative to an array of sensors used to sense the effect of the signals. The position of an anomaly (e.g., lesion, tumor, cyst) is optionally determined according to at least one surface map generated by the array of sensors in relation to the positions of the specific points from which the electrifying signals are applied. In some embodiments of the invention, the electrifying signals are applied to a small region relative to the area of the array of sensors.

In some embodiments of the present invention, the electrifying signals are applied in a specific spatial pattern which increases the signal to noise ratio in the array of sensors of signals originating from anomalies which are to be detected. In some embodiments of the invention in which the signals are applied from a surface opposite the sensors, the dimensionality of the applied signals is reduced so that deep anomalies receive stronger signals than anomalies close to the sensors. For example, instead of applying signals from an entire surface, signals are applied along a line, from a single point, or in the form of a dipole.

Optionally, the electrifying signals are applied in lines which are long and narrow relative to the size of an average anomaly. The long and narrow lines have at least a 1:5 ratio between width and length, optionally at least a 1:8 ratio. In some embodiments of the invention, the long and narrow lines are generated by an array of substantially square electrodes organized in a line. Alternatively or additionally, the electrifying signals are applied in other patterns and sizes, such as, large and small rings, circles, squares and rectangles. Further alternatively or additionally, electrifying signals are applied in a few geometrically unconnected regions.

In some embodiments of the present invention, the electrifying signals are applied in a form which includes signals with different phases in a predetermined spatial relationship, e.g., with substantially opposite polarities. Optionally, the applied signals are in the form of a dipole. In some embodiments of the invention, the electrifying signals are in the form of two parallel straight lines which have opposite and equal polarities. The distance between the lines forming the dipole is optionally adjustable.

An aspect of some embodiments of the present invention relates to applying high frequency electrifying signals for impedance imaging of a body portion by an array of sensors used to sense the effect of the applied signals. The term high frequencies relates to frequencies of at least the order of thousands of Hz, particularly frequencies above about 30-40 kHz. In some embodiments of the invention, higher frequencies, for example, above 100 kHz, are

used. Although the use of high frequencies requires more sophisticated apparatus than required for low frequencies, the use of high frequencies in impedance imaging reduces the masking effect of the skin surface.

An aspect of some embodiments of the present invention relates to determining the depth of an anomaly within an organ. In some embodiments of the invention, the depth is determined by inducing an electrical dipole of known orientation within the anomaly. The dipole within the anomaly induces a dipole field within the organ and this field influences the sensed values of the multi-element probe. When the dipole within the anomaly causes a field perpendicular to the probe it induces a peak within the sensors. The location and strength of the peak are indicative of the location of the anomaly. When the direction of the field of the dipole within the anomaly is parallel to the multi-element probe, the dipole induces two peaks within the sensors and the distance between the peaks is indicative of the depth of the anomaly within the organ.

The position of an anomaly, including its depth, is optionally determined based on a plurality of impedance maps. Optionally, the plurality of impedance maps are generated responsive to respective electrifying patterns which are applied in a manner systematically covering a surface of the imaged body part.

In some embodiments of the present invention, the body part, which is for example a breast, is pressed between a pair of multi-element probes. Optionally, one of the probes serves as an electrifying probe which provides electrifying signals to the breast and the other probe serves as the array of sensors. The patterns of electrifying signals are optionally provided by activating specific elements or groups of elements of the electrifying probe.

An aspect of some embodiments of the present invention relates to a method of sensing the electric field in impedance imaging while the influence of the sensors on the field is minimized. In some embodiments of the present invention, the array of sensors senses voltages using sensors with a high input impedance.

In some embodiments of the present invention, the electrifying signals are sensed at any single time only by a sub-group of the sensors on the probe. Optionally, a single map covering substantially all the sensors of the probe is generated in a plurality of steps, each step including sensing from a different sub-group of the sensors. Optionally, those sensors not presently used in generating the map are kept floating so that they do not affect the currents in the body part. In some embodiments of the invention, only a small percentage of the sensors of the sensing array are active when readings are taken by the sensor array. In some embodiments

of the invention, the array of sensors comprises low impedance sensors which measure currents and most of the sensors are kept floating when a reading is taken. Therefore, the sensors do not force the currents to be perpendicular to the sensors and only nominally affect the electric fields in the organ.

In some embodiments of the invention, in each step a subset of sensors which are used in producing the map are chosen according to the location, size, frequency and/or any other attribute of the electrifying signals. Alternatively, the subsets for each step are chosen so as to sequentially cover the entire area of the probe.

An aspect of some embodiments of the present invention relates to normalizing the generated map so as to remove an uneven direct effect of the electrifying signals on the map. Optionally, a normalizing value is subtracted from each area which receives equal direct effect from the electrifying signals. For example, when the electrifying signals are applied along straight lines the normalizing values are calculated for each line. Optionally, the normalizing values are calculated as the average of all the sensed values in the area from which the normalized value is subtracted.

An aspect of some embodiments of the present invention relates to generating electrifying signals for impedance imaging from an invasive tool within an organ being imaged. In some embodiments of the present invention, one or more sensing probes pressed against a surface detect the signals from the invasive tool, as the tool is moved toward an anomaly. As the invasive tool approaches the anomaly, the effect of the anomaly on the charge induced within the anomaly and thus on signals sensed by the sensing probe is enhanced. Thus, the image formed by the sensing probe can be used to monitor, manually or automatically, the movements of the probe toward the anomaly. When the invasive tool touches or enters the anomaly, the direct electrification of the anomaly by the tool induces a detectable change in the signals sensed due to the anomaly.

In some embodiments of this aspect, an additional surface probe is used to apply a signal with opposite polarity from the signal from the invasive tool. Thus, a dipole is induced within the anomaly, allowing easier detection of the signals from the anomaly. When the invasive tool is very close to (or touches) the anomaly the polarity of the dipole in the anomaly changes, providing additional indication of the proximity of the tool to the anomaly.

In some embodiments of the present invention, the phases of the applied signals from the surface probe with respect to those of the invasive tool are changed during the insertion in order to induce additional detectable changes in the dipole of the anomaly.

An aspect of some embodiments of the present invention relates to determining the orientation of an invasive tool within an organ. Optionally, a single electric voltage level is applied to the invasive tool over an entire length which is being tracked. The width of the tool in the surface map is indicative of the depth of the tool. The orientation of the tool is optionally determined from the difference in the width of the tool in the surface map along the length of the tool and its orientation on the surface map.

In some embodiments of the present invention, external probes are used to induce a monotonously changing-with-position electric field within the organ. When an electric voltage is applied to the needle within the region, the needle appears brighter than its surroundings in those areas in which the needle has a higher voltage than its surroundings. On the other hand, in areas in which the needle is at a lower voltage than its surroundings the needle appears darker than its surroundings. In some embodiments, the voltage applied to the needle is varied until the needle appears most clearly relative to the surroundings and/or until the depth and/or orientation of the needle are most easily determined.

There is therefore provided in accordance with an embodiment of the present invention, apparatus for impedance imaging of a region within a subject, comprising a plurality of electrodes adapted to, substantially concurrently, apply electrical signals having a common frequency and different phases to the subject and a plurality of sensing elements adapted to sense electrical signals from a surface of the region, responsive to signals applied from the electrodes. Optionally, the plurality of sensing elements are included in a multi-element probe including a two-dimensional array of sensing elements. Possibly the apparatus includes a screen for displaying an image of the region responsive to signals sensed by the sensing element. Optionally, the screen is adapted to display an image which represents a projection of the region on to the multi-element probe. Possibly the apparatus includes a sensing controller adapted to initiate sensing by at least one of the sensing elements while at least one of the sensing elements is kept electrically floating.

Optionally, the plurality of electrodes are adapted to apply signals with opposite phases to the subject. Alternatively or additionally, plurality of electrodes are adapted to apply signals with equal amplitudes to the subject. Further alternatively or additionally, the plurality of electrodes are adapted to apply signals with frequencies above 40KHz to the subject.

In some embodiments of the invention, the plurality of electrodes are adapted to apply signals in the form of at least one dipole to the subject. Alternatively or additionally, the plurality of electrodes are adapted to apply signals in the form of at least one long and narrow

line to the subject. Possibly the apparatus includes a processing unit adapted to determine a depth of an anomaly beneath the sensing elements responsive to the sensed signals. Optionally, the processing unit is adapted to determine a distance between peaks on a map of the sensed signals. Optionally, the plurality of electrodes are included in an electrode probe and wherein the apparatus includes a controller adapted to electrify less than all the electrodes of the electrode probe. In some embodiments of the invention, at least one of the plurality of sensing elements has a high input impedance.

There is further provided in accordance with an embodiment of the present invention, apparatus for impedance imaging of a region within a subject, comprising a multi-element probe comprising a plurality of electrifyable elements adapted to apply electrical signals to the region, an electrification controller adapted to electrify a group including at least one long and narrow line of the electrifyable elements of the probe, but less than all the electrifyable elements and a plurality of sensing elements adapted to sense electrical signals from the region, responsive to signals applied by the electrodes.

Optionally, the probe comprises a two-dimensional array of electrifyable elements and the electrification controller is adapted to electrify at least one column or row of the elements of the probe. Optionally, the electrification controller is adapted to sequentially apply electrical signals to lines of elements of the multi-element probe. Alternatively or additionally, the electrification controller is adapted to electrify concurrently at least two rows or lines of the elements of the multi-element probe.

Optionally, the electrification controller is adapted to apply electrical signals to parallel pairs of lines of elements of the multi-element probe. Optionally, the electrification controller electrifies concurrently at least two rows or lines of the probe, with signals having different amplitudes, frequencies or phases. Optionally, plurality of sensing elements are included in a multi-element probe including a two-dimensional array of sensing elements. Optionally, at least some of the sensing elements are held at an equipotential level. Optionally, the apparatus includes an analysis unit which analyses the region responsive to signals sensed by the sensing elements. In some embodiments of the invention, the analysis unit analyses the region also responsive to the positions of the electrodes applying the electrical signals. Optionally, the analysis unit determines at least one characteristic of an anomaly within the region. Alternatively or additionally, the analysis unit determines a depth of an anomaly within the region. Optionally, the electrification controller is capable of determining a medical diagnosis of the anomaly. Optionally, the analysis unit is capable of determining whether an anomaly

exits in the region. In some embodiments of the invention, the multi-element probe is mounted on an invasive tool adapted to be inserted into the region. Optionally, the plurality of sensing elements are mounted on an invasive tool adapted to be inserted into the region. Optionally, the electrification controller generates a current tracing map responsive to the measured signals. In some embodiments of the invention, the electrification controller normalizes the current tracing map. Optionally, the electrification controller normalizes the map by subtracting background values from the generated map. Optionally, the electrification controller normalizes the map by subtracting, from the measured signals of at least one group of elements, a representative value of the group. Optionally, the plurality of electrifyable elements are adapted to apply signals at frequencies above 40 kHz.

There is further provided in accordance with an embodiment of the present invention, apparatus for impedance imaging of a region, comprising an electrifying probe which applies a plurality of distinct electrifying signals to the region, and a sensing probe, comprising a two dimensional array of sensing elements which sense signals generated responsive to the plurality of distinct electrifying signals. Optionally, the plurality of distinct electrifying signals are of substantially the same frequency and/or amplitude. Optionally, the plurality of distinct electrifying signals have different phases.

There is further provided in accordance with an embodiment of the present invention, apparatus for impedance imaging of a region, comprising at least one first electrode adapted to apply currents to the region, at least one second electrode adapted to attract currents from the region, a probe, comprising a plurality of sensing elements for sensing signals induced by the applied currents, and circuitry which is adapted to measure signals from a plurality of the sensing elements and generate an impedance map based on the differences between the measurements of pairs of adjacent sensing elements.

Optionally, the at least one second electrode and the at least one first electrode are adapted to be positioned on opposite sides of the region. Optionally, the probe comprises at least one sensing element having a high input impedance. Optionally, the probe comprises at least one sensing element having a low input impedance. Optionally, the probe comprises at least one sensing element having a controllable input impedance. Optionally, the probe comprises at least one pair of sensing elements which are separated by less than a centimeter.

There is further provided in accordance with an embodiment of the present invention, apparatus for sensing electrical signals from a tissue surface, comprising at least one contact

surface suitable for contact with the tissue surface; and a sensing circuit with a controllable input impedance, which senses electrical signals incident on the at least one contact surface.

Optionally, the sensing circuit comprises one or more switches which select one of a plurality of predetermined input impedance values. Optionally, the input impedance of the sensing circuit may be set to a substantially zero input impedance and/or a substantially infinite input impedance. In some embodiments of the invention, the at least one contact surface comprises at least one sharp edge which penetrates an upper layer of the tissue surface. Optionally, the at least one contact surface comprises a flat surface.

There is further provided in accordance with an embodiment of the present invention, apparatus for sensing electrical signals from a tissue surface, comprising a two dimensional array of sensing elements, at least one of the sensing elements has a high input impedance; and circuitry which generates an impedance map responsive to signals sensed by the sensing elements. Optionally, substantially all the sensing elements have a high input impedance.

Optionally, the at least one sensing element with a high input impedance comprises at least one sharp edge which penetrates an upper layer of the tissue surface.

There is further provided in accordance with an embodiment of the present invention, apparatus for impedance imaging of a region within a subject, comprising at least one electrifyable element capable of electrifying the subject, a multi-element probe, comprising a plurality of sensing elements, capable of measuring signals from the region, circuitry capable of generating a map from the signals sensed by the sensing elements; and a processing unit adapted to determine a depth of an anomaly beneath the multi-element probe responsive to the generated map. Optionally, the at least one electrifyable element is adapted to apply electrical signals with different phases to the subject. Optionally, the processing unit determines a distance between two peaks on the map. Optionally, the processing unit is adapted to determine a point on the map above the anomaly, responsive to the generated map.

There is further provided in accordance with an embodiment of the present invention, apparatus for determining a location of an elongate object in a region of a subject, comprising at least one surface probe adapted to induce an electrical condition in the region, a multi-element probe adapted to sense electrical signals from a surface of the region, circuitry adapted to generate an impedance map responsive to signals sensed by the multi-element probe, a power source adapted to apply electrical signals to the elongate object, and a controller adapted to adjust at least one parameter of the electrical signals provided to the

elongate object, such that the location of the elongate object in the region may be determined responsive to an imprint of signals from the elongate object on the impedance map.

Optionally, the controller automatically adjusts the at least one parameter responsive to the impedance map. Optionally, the controller provides an indication when the location of the elongate object in the region may be determined responsive to the imprint of signals from the elongate object on the impedance map. Alternatively or additionally, the controller provides an indication when the imprint of the elongate object on the map has a lower amplitude than surrounding signals at a first portion of the map and a higher amplitude than surrounding signals at a second portion of the map. Optionally, the controller is adapted to determine a depth of the elongate object responsive to the signals applied to the elongate object.

There is further provided in accordance with an embodiment of the present invention, apparatus for impedance imaging of a region within a subject, comprising an electrification probe adapted to apply electrifying signals at a plurality of distinct frequencies to the region through different respective electrifying elements, a sensing probe, comprising a plurality of sensing elements, adapted to sense signals from a surface of the region responsive to electrifying signals applied to the region by the electrification probe, and circuitry adapted to create a plurality of maps for the distinct frequencies responsive to signals sensed by the sensing elements.

Optionally, the sensing probe is adapted to sense signals a predetermined number of times during a sensing period and wherein the number of distinct frequencies comprises substantially the maximal number allowed by the predetermined number of samplings according to Nyquist's law. Optionally, the circuitry generates the plurality of maps using a single FFT operation.

There is further provided in accordance with an embodiment of the present invention, a method of impedance imaging of a region within a subject, comprising positioning a first multi-element probe, comprising a plurality of sensing elements, on one side of the region, positioning a second multi-element probe including a plurality of electrifyable elements on a second side of the region, electrifying at least one of the plurality of electrifyable elements forming a long and narrow line, but less than all the electrifyable elements, and measuring a signal at at least some of the sensing elements.

Optionally, the method includes sequentially electrifying and measuring while electrifying different sub-groups of elements of the second multi-element probe. Optionally, sequentially electrifying comprises sequentially electrifying pairs of one-dimensional strips of

the second multi-element probe. Optionally, sequentially electrifying the pairs of one-dimensional strips comprises electrifying the one-dimensional strips with signals of respective opposite polarities. In some embodiments of the invention, electrifying the pairs of one-dimensional strips comprises electrifying pairs of one-dimensional strips which are separated by a predetermined distance, to form a dipole source of electrification.

Optionally, the method includes analyzing the region responsive to the measured signals and the positions of the electrified elements. Optionally, the electrified elements cover an area which is less than ten percent of a face area of the multi-element probe. Optionally, positioning the electrifyable elements comprises mounting the electrifyable elements on an invasive tool inserted into the region. Optionally, electrifying the electrifyable elements comprises applying at least two electrifying signals with different phases.

In some embodiments of the invention, applying the at least two electrifying signals comprises applying signals of substantially opposite polarity. In some embodiments of the invention, positioning the multi-element probe comprises holding substantially all of the sensing elements of the first multi-element probe at a same potential.

There is further provided in accordance with an embodiment of the present invention, a method of impedance imaging of a region, comprising positioning a multi-element probe, comprising a plurality of sensing elements, on a surface of the region, providing an electrifying field to the region substantially in the form of a dipole, and measuring a signal at at least some of the elements of the multi-element probe responsive to the electrifying field.

Optionally, providing the dipole electrifying field comprises providing signals of opposite polarity to spaced electrifyable elements. Optionally, providing the electrifying field comprises providing the field from a dipole formed of parallel lines.

There is further provided in accordance with an embodiment of the present invention, a method of impedance imaging of a region, comprising positioning a multi-element probe, comprising a plurality of sensing elements, on a surface of the region, providing a plurality of electrifying fields of different phases to the region and measuring a signal at at least some of the elements of the multi-element probe responsive to the electrifying fields.

Optionally, providing the plurality of electrifying fields comprises providing fields which comprise a dipole field. Optionally, providing the plurality of electrifying signals comprises providing signals which have voltages such that the sum of the voltages of the signals is substantially zero at substantially any time.

There is further provided in accordance with an embodiment of the present invention, a method of impedance imaging of a region, comprising positioning a multi-element probe, comprising a plurality of sensing elements, on a surface of the region, applying an electrical field to the region, connecting at least some of the sensing elements of the multi-element probe to a sensor through a high input impedance, measuring an electrical signal produced by at least some of the sensing elements with the high input impedance sensor, and producing an impedance map responsive to the difference between the measured signals of pairs of at least some of the sensing elements.

Optionally, applying the electrical field comprises applying signals to a pair of electrodes on substantially opposite sides of the region. Optionally, applying the signals to the pair of electrodes comprises applying signals to a pair of electrodes positioned such that a straight line connecting the electrodes is substantially parallel to the multi-element probe. In some embodiments of the invention, applying the signals to the pair of electrodes comprises applying signals to a pair of electrodes positioned substantially perpendicular to the multi-element probe. Optionally, applying the signals to the pair of electrodes comprises applying signals to a pair of electrodes such that the combined field produced by electrification of the pair of electrodes is substantially parallel to the multi-element probe.

Optionally, applying the signals comprises applying signals of a different amplitude to each of the electrodes. Alternatively or additionally, applying the signals to the pair of electrodes comprises holding one of the electrodes at a ground potential.

There is further provided in accordance with an embodiment of the present invention, a method of impedance imaging of a region, comprising positioning a multi-element probe, comprising a plurality of adjacent sensing elements, on a surface of the region, positioning a pair of electrodes on substantially opposite sides of the region, electrifying the pair of electrodes to provide an electrical field between the pair of electrodes, measuring an electrical signal by at least some of the sensing elements responsive to the electrifying of the pair of electrodes, and producing an impedance map of the region responsive to the difference between the signals measured by adjacent sensing elements.

There is further provided in accordance with an embodiment of the present invention, a method of determining the position of an anomaly within a region of a body, comprising applying electrifying signals to the region, determining a response map along a surface of the region responsive to the applied signals, determining a point on the surface which is above the

anomaly responsive to the response map, and calculating a depth from the determined point to the anomaly responsive to the response map.

Optionally, determining the response map comprises determining a map which covers less than half the total surface area of the region. Alternatively or additionally, determining the response map comprises determining a plurality of maps generated responsive to different patterns of electrifying signals. Optionally, determining the point above the anomaly comprises finding a point located between a pair of peaks on the map.

Optionally, calculating the depth comprises determining a distance between the pair of peaks. Optionally, applying electrifying signals to the region comprises inducing a dipole which is substantially parallel to the surface along which the response map is determined.

There is further provided in accordance with an embodiment of the present invention, a method of impedance imaging of a region, comprising positioning a probe, comprising a plurality of sensing elements, on a surface of the region, simultaneously applying electrifying signals at a plurality of distinct frequencies to the region through different electrifying elements, and measuring electrical signals by at least some of the sensing elements responsive to the applied electrifying signals.

Optionally, the method includes determining a separate influence on the region, of the signals of at least one of the distinct frequencies responsive to the measured signals.

In some embodiments of the invention, measuring the electrical signals comprises sampling signals by the sensing elements a predetermined number of times and wherein the number of distinct frequencies comprises substantially the maximal number allowed by the predetermined number of samplings according to Nyquist's law. Optionally, the method includes selecting a plurality of beginning frequencies and adjusting the frequencies so as to fit into nearest vacant Nyquist bins in order to receive the distinct frequencies.

Optionally, selecting the plurality of beginning frequencies comprises selecting based on physiological characteristics of the region. Optionally, adjusting the frequencies comprises adjusting low frequencies before high frequencies. Optionally, applying electrifying signals at a plurality of distinct frequencies comprises applying signals at frequencies only within a narrow band in which impedance measures do not change substantially.

Optionally, simultaneously applying electrifying signals at a plurality of distinct frequencies comprises placing an electrification probe including an array of electrodes on a surface of the region and electrifying different electrodes of the array with different

frequencies. Optionally, the method includes generating separate maps for a plurality of the distinct frequencies responsive to the measured electrical signals.

In some embodiments of the invention, generating the separate maps is performed using a single FFT operation. Optionally, the distinct frequencies are selected so as to allow generating the separate maps using the single FFT operation. In some embodiments of the invention, generating the separate maps is performed using algebraic operations.

There is further provided in accordance with an embodiment of the present invention, a method of guiding an elongate object within a region of a subject, comprising providing electrifying signals to at least a part of the elongate object within the region, providing electrifying signals, different from the signals provided to the at least a part of the elongate object, from a surface of the region, measuring electrical signals on a surface of the region, moving the elongate object, comparing the electrical signals measured on the surface of the region before and after the movement, and determining desired movements of the object responsive to the comparison. Optionally, providing the electrifying signals from the surface comprises providing signals of opposite polarity of the signals provided to the elongate object. Optionally, the elongate object comprises a biopsy needle. Optionally, providing the electrifying signals comprises providing the signals to a probe mounted on the elongate object. Alternatively, providing the electrifying signals comprises electrifying the elongate object. Optionally, determining the desired movements comprises determining a movement direction which enhances the measured signals.

There is further provided in accordance with an embodiment of the present invention, a method for determining the location of an elongate object in a region of a subject, comprising providing electrifying signals to at least a part of the elongate object within the region, measuring electrical signals on a surface of the region, and providing an indication responsive to a reversal of the polarity of the measured signals.

There is further provided in accordance with an embodiment of the present invention, a method for determining the location of an elongate object in a region of a subject, comprising providing electrifying signals to at least a part of the elongate object within the region, measuring electrical signals on a surface of the region, and determining a depth of a plurality of points along the elongate object, relative to the surface from which the signals are measured, responsive to the measured signals.

Optionally, measuring the electrical signals comprises producing a two dimensional map of signals on the surface of the region. Optionally, determining the location of the object

comprises determining a depth of the object responsive to the width of an image of the object on the two dimensional map. Optionally, determining the location of the object comprises determining a depth of the object responsive to the strength of the signals on the two dimensional map. Optionally, the method includes providing electrifying signals to the region from a surface of the region. Optionally, the method includes varying the amplitude of the signals provided to the at least part of the elongate object.

Optionally, determining the location of the object comprises generating a two dimensional map responsive to the measured signals and determining an amplitude of the electrifying signals provided to the object at which at least part of an image of the object on the map is not distinguishable from its surroundings.

In some embodiments of the invention, determining the location of the object comprises generating a two dimensional map responsive to the measured signals and determining an amplitude of the electrifying signals provided to the object at which at least part of an image of the object is darker than its surroundings on the map and at least part of the image of the object is brighter than its surroundings on the map.

There is further provided in accordance with an embodiment of the present invention, a method for determining a location of an elongate object in a region of a subject, comprising providing electrifying signals to a part of the elongate object within the region, measuring electrical signals on a surface of the region, generating a map of the region responsive to the measured signals, and changing the electrical signals provided to the elongate object so that the surface signals generated responsive to the signals provided to the elongate object are lower than surrounding surface signals on the map at a first portion of the map and higher than surrounding surface signals on the map at a second portion of the map.

Optionally, changing the electrical signals comprises changing an amplitude of the signals. Optionally, determining the location of the object comprises determining a depth of the object responsive to the amplitude of the changed signals.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will be more clearly understood from the following detailed description of embodiments of the invention and from the attached drawings, in which same number designations are maintained throughout the figures for each element and in which:

Fig. 1 is a perspective view of an imaging head suitable for breast impedance mapping in accordance with an embodiment of the invention;

Fig. 2 is a schematic side view of the imaging head of Fig. 1 during an imaging procedure, in accordance with an embodiment of the present invention;

Fig. 3A is a two-dimensional schematic graph of current sensed from a healthy breast, in accordance with an embodiment of the present invention, when the breast is electrified by a linear dipole;

Fig. 3B is a two-dimensional schematic graph of signals sensed from a breast with an anomaly, in accordance with an embodiment of the invention, under conditions similar to those of Fig. 3A;

Fig. 3C is a schematic normalized graph of the graph of Fig. 3B, in accordance with an embodiment of the present invention;

Figs. 4A-C are schematic illustrations of an imaging stage using electrifying elements forming a dipole in which an anomaly is at different locations relative to the dipole, in accordance with another embodiment of the present invention;

Fig. 5 is a schematic illustration of a sensor, in accordance with an embodiment of the present invention;

Fig. 6 is a schematic illustration of an impedance imaging system, in accordance with an embodiment of the present invention;

Fig. 7 is a schematic illustration of leading a needle, using impedance imaging control, in accordance with another embodiment of the present invention; and

Fig. 8 is a schematic illustration of an invasive tool, in accordance with an embodiment of the present invention.

DETAILED DESCRIPTION OF EMBODIMENTS

Fig. 1 illustrates an impedance image head 12 suitable for mapping the impedance of a breast, in accordance with an embodiment of the present invention. Head 12 optionally comprises a lower plate probe 22 and an upper plate probe 24. The lower or upper plate (or both) is optionally mounted on a pair of rails 26 to allow the distance between plate probes 22 and 24 to be varied. Movement of probe 22 along rails 26 may be achieved by a motor (not shown) or by hand.

Either or both of plate probes 22 and 24 are provided with multi-element probes 28 and 30 respectively, which electrically contact the breast with a plurality of sensing elements 48. Sensing elements 48 are used to provide electrical excitation to the breast and/or to measure signals generated responsive to the provided excitation. In some embodiments of the invention, sensing elements 48 are organized in a two dimensional array. Sensing elements 48

are optionally separated by a small distance, for example of the order of 0.1 millimeters, in order to allow generation of high precision images.

In some embodiments of the invention, sensing elements 48 comprise flat surfaces which contact the breast. Alternatively, sensing elements 48 comprise sharp points which penetrate an upper layer of the skin of the breast, so as to reduce the masking effect of the skin. The use of sharp points is especially advantageous when sensing elements 48 are used with high input impedances for voltage measurements, as described hereinbelow. In such embodiments, the different penetration depths involve small measurement differences between sensing elements 48 relative to the input impedance of the sensing elements.

Probes 28 and 30 are optionally as described in U.S. patent 5,810,742, although other types of probes may be used.

In some embodiments of the present invention, the elements 48 of probe 30 provide electrical excitation and elements 48 of probe 28 measure signals responsive to the provided excitation. Alternatively or additionally, in a first stage, elements 48 of probe 30 provide electrical excitation and elements 48 of probe 28 measure the signals, and in a second stage the elements 48 of probe 30 measure signals and elements 48 of probe 28 provide the electrical excitation. Further alternatively or additionally, some of elements 48 of a single probe 28 and/or 30 provide electrical excitation while, simultaneously, other elements 48 of the same probe measure the signals. Further alternatively or additionally, excitation is provided from a third, possibly remote point, and both probes 28 and 30 sense the resultant signals, concurrently and/or sequentially.

In some embodiments of the present invention, elements 48 are electrified using multi-frequency transmitters and the signals which elements 48 sense are received by a multi-frequency receiver. Thus, a plurality of different scanning steps using different frequencies may be performed simultaneously. It is noted that the human body responds linearly to the signals, i.e., does not mix signals of different frequencies. In an embodiment of the present invention, each electrification step is performed by electrifying the same elements with signals of a combination of frequencies. In an embodiment, signals of different frequencies are applied to different groups of elements 48. Alternatively or additionally, signals combined from a few different frequencies are applied to one or more elements 48.

In an embodiment of the present invention, the multi-frequency signals are applied using a look up table which prepares the digital values of the signals and an analog to digital converter.

The number of different frequencies used concurrently depends on the number of samplings performed by those elements 48 which are used for sampling. In some embodiments of the invention, the number of distinct frequencies x is the maximal allowed by Nyquist's law. According to Nyquist's law, if N samplings of each element 48 are used in preparing an image, the maximal value of x is N/2. However, since the amplitude of the DC frequency cannot be determined x is optionally N/2-1.

In some embodiments of the present invention, the x frequencies to be used simultaneously are selected so as to allow fast conversion of the sampled signals into frequency distinct maps. Optionally, the x frequencies are chosen in a manner which allows the sensed signals to be converted into a plurality of frequency distinct images using a single Fast Fourier Transform (FFT).

In some embodiments of the invention, each of sensing elements 48 is controlled separately (or the elements are controlled in groups) such that at any single moment some of elements 48 may measure signals, others may provide excitation, and still others may be passive. Optionally, elements 48 which provide excitation may be driven separately, such that at a single moment different elements 48 of probe 30 provide signals at different amplitudes, frequencies and/or relative phases. Alternatively or additionally, groups of elements 48 forming predetermined shapes on probe 30, are driven together. In some embodiments of the present invention, elements 48 in a single column 36 (or in a single row) are controlled together.

Alternatively or additionally, probe 30 comprises an array of elements of the sizes and/or shapes in which the electrifying signals are to be applied. In some embodiments of the present invention, probe 30 comprises a one-dimensional array of elongated elements. Alternatively or additionally, probe 30 comprises elements of other shapes useful in applying the signals, such as, radial and/or sectorial elements. In some embodiments of the present invention, probe 30 is not necessarily rectangular, but rather is of another shape, such as a circular shape, in order to conform to the shape of the elements.

Head 12 is optionally provided with a pivot (not shown) to allow for arbitrary rotation of the head about one or more of its axes. This allows for both medio-lateral and cranio-caudal maps of the breast to be acquired, at any angular orientation about the breast. Head 12 may be tilted so that the surfaces of plate probes 22 and 24 are oriented with a substantial vertical component so that gravity assists the entry of the breast into the space between the maximum

extent and to keep it from inadvertently falling out. This is especially useful when the patient leans over the plates so that her breasts are positioned downwardly between the plate probes.

In some embodiments of the present invention, one or both of probes 28 and 30 may be rotated about an axis at one end thereof, by a rotation mechanism 27 on their associated plate probes 22 or 24, such as shown in Fig. 1 for probe 28. Alternatively or additionally, probes 28 and/or 30 may be slidable, as for example along members 31.

Such additional sliding and rotating flexibility is useful for providing more intimate skin contact of the probes with the breast, which has a generally conical shape. Furthermore, such flexibility allows for better imaging of the areas of the breast near the chest wall or the rib cage, which are extremely difficult to image in x-ray mammography.

In practice, a breast is inserted between probes 28 and 30 and plate probe 22 is raised, or plate probe 24 is lowered, to compress the breast between the probe. This compression reduces the distance between the probes and provides better contact between the sensing elements and the skin of the breast. Although compression is desirable, the degree of compression required for impedance imaging is much lower than required for X-ray mammography. Alternatively or additionally, probes 28 and/or 30 are curved to conform with the surface of the breast in a non-planar fashion.

It is noted that for reasons of clarity, Figs. 2, 4A, 4B, 4C and 6 show a gap between breast 40 and probes 28 and 30. This gap is not normally existent during impedance imaging procedures.

An imaging procedure optionally comprises a plurality of stages. In a first stage, the breast is scanned in order to determine whether there is a suspected anomaly within the breast. An optional method for performing the scanning of the first stage is described hereinbelow in relation to Figs. 2 and 3A-3C. In a second stage, the precise location of the suspected anomaly is found, in particular the depth of the anomaly from either or both of probes 28 and 30. An optional method for determining the depth is described hereinbelow with reference to Figs. 4A-4C. In a third stage, electrification measurements are used to determine the type of the anomaly, i.e., whether the anomaly is cancerous or otherwise requires treatment. If the tests of the third stage indicate that invasive tests of the anomaly are required, a fourth stage is optionally performed in which impedance imaging is used to direct an invasive tool, such as a biopsy needle, toward the anomaly. An optional method for leading an invasive tool toward the anomaly is described hereinbelow with reference to Fig. 7.

Fig. 2 is a schematic side view of impedance imaging head 12 during an imaging procedure of a breast 40, in accordance with an embodiment of the present invention. Optionally, the imaging procedure comprises a plurality of steps in which one or more elements 48 of probe 30 apply electrical excitation to breast 40. In an embodiment of the invention, probe 28 is kept at a (virtual) ground voltage level, or another equipotential, such that electrical current flows from the electrified elements 48 of probe 30 towards probe 28. Substantially all of elements 48 of probe 28 (referred to herein as sensors 34) sense the electrical signals reaching a surface 42 of breast 40, and a two dimensional map of these electrical signals is prepared (this map is referred to herein as a current tracing map).

In some embodiments of the present invention, one or a few closely spaced sensing elements on one of the probes is electrified, and the others are left floating. This would cause a beam-like flow of current from the electrified elements to the other sensing elements on the other probe. The anomaly would disturb this flow causing impedance variations which are strongest for those elements which are in the path of the current disturbed by the object. If a number of such measurements are made, each with a different group of electrodes being electrified, then good information regarding the three dimensions of the position of the object can be obtained.

In some embodiments of the invention, the applied electrical signals comprise voltage and/or current signals suitable for impedance imaging of breast 40, as described for example in US patent 5,810,742. In some embodiments of the present invention, the signals are AC signals of frequencies of 0.1-10 MHz, for example 500 kHz. Alternatively or additionally, the applied signals have higher or lower frequencies, for example between about 1-50 kHz. Further alternatively or additionally, the applied signals comprise DC signals.

In some embodiments of the present invention, in each step of the imaging procedure a different column 36 of elements 48 is electrified, while the rest of elements 48 of probe 30 are left floating. Optionally, during an entire imaging procedure each column 36 is electrified once. For example, columns 36 are electrified sequentially from left to right or from right to left in Fig. 2. In some embodiments of the present invention, those columns 36 which are far from a suspected anomaly are skipped.

Alternatively or additionally, elements 48 of probe 30 are electrified in other groups, such as along rows perpendicular to columns 36, along diagonal lines, and/or in concentric circles or ellipses. In some embodiments of the invention, the groups do not include common elements 48. Optionally, each element 48 is included in at least one group. In some

embodiments of the invention, each of the groups covers only a small area of probe 30, optionally less than 10% of the probe.

Applying signals from a small area relative to the area of probe 28 at which the signals are sensed, makes signals from surface anomalies close to sensing probe 28 (which are generally less interesting) interfere less with signals from a deep anomaly, the location of which is being determined. In addition, the sensed signals which are indicative of the deep anomaly vary according to the position of the electrifying group, while the signals indicative of the surface anomaly which is close to probe 28 do not change with the position of the electrifying group.

Reference is also made to Figs. 3A and 3B which are two-dimensional schematic graphs 60 and 64 of the current sensed by probe 28, in accordance with an embodiment of the present invention. Figs. 3A and 3B show graphs sensed from breast 40 when electrifying signals are applied along a line 36' of elements 48 (Fig. 2). Graph 60 in Fig. 3A shows the signals sensed from a healthy breast. The current sensed by sensors 34 of probe 28 (Fig. 2) is inversely proportional to the distance between the sensors and the electrifying elements along line 36'. Therefore, graph 60 has a peak 62 along a line parallel to line 36' which declines as the distance from line 36' increases. Graph 60 has substantially identical values along lines parallel to line 36' due to the regularity of the tissue of a healthy breast 40.

Graph 64 in Fig. 3B shows the current sensed from a breast which has an anomaly 46 within it. The impedance of the tissue of anomaly 46 is substantially different from the impedance of the healthy tissue of breast 40. The electric field caused by the current from line 36' induces a dipole within anomaly 46. Therefore, in addition to a peak 62 similar to the one in graph 60, graph 64 includes a peak 66 induced by the dipole in anomaly 46. The heights of peaks 62 and 66 depend on the amplitudes and frequencies of the signals applied along line 36', as well as on the tissue characteristics of anomaly 46. The height and width of peak 66 also depends on the depth of anomaly 46 within breast 40. This is because the electric field of anomaly 46 declines with the third power of the distance between anomaly 46 and surface 42. The height of peak 66 also depends on the induced dipole moment of anomaly 46. In some embodiments of the invention, the dipole moment of anomaly 46 is estimated from the type and/or shape of the anomaly. The depth of anomaly 46 within breast 40 is optionally determined based on the estimated dipole moment and on the relative height of peak 66 relative to peak 62. Alternatively or additionally, anomaly 46 is assumed to have a regular spherical shape.

In some embodiments of the present invention, impedance graphs 64 are generated on both probes 28 and 30 and the depth of anomaly 46 is estimated from the relative heights of peaks 66 on the opposing graphs. In some embodiments of the invention, the sensing elements of one of probes 28 and 30 are all electronically floating and are not in use, while the elements of the other of probes 28 and 30 operate as sensors, and a remote signal source is used to electrify breast 40. After an image is obtained from the one probe, the roles of the two probes 28 and 30 are reversed to obtain an image from the other probe.

Alternatively, if all the elements 48 of one of the probes are electrified to the same voltage and the measuring probe is kept at a virtual ground, the currents drawn from and received by the elements of both probes form a two dimensional admittance image of the region between the probes.

In some embodiments of the invention, the graph sensed by probe 28 is normalized in a manner which eliminates the effects resulting directly from line 36'. In some embodiments of the present invention, currents which appear along the entire length 65 of graph 64 are subtracted from the graph. Since it is reasonable to assume that anomaly 46 does not extend along the entire length of lines 36, currents which appear along the entire length 65 of graph 64 are not indicative of anomaly 46 and generally result directly from line 36'. Optionally, a normalizing value is subtracted from the values of each line 38 of sensors 34 parallel to lines 36. In some embodiments of the invention, the normalizing value for each line 38 comprises the average or mean value sensed along line 38. Alternatively, the normalizing value comprises the minimum value sensed by any of the sensors 34 along line 38. The minimum value is common to all the sensors 34 along the line and therefore does not result from anomaly 46. In some embodiments of the present invention, when an anomaly 46 is detected, either automatically or by a physician, the normalizing value is an average of the values along lines 38 of those points which do not belong to the anomaly.

Alternatively, an expected set of values for healthy tissue is subtracted from graph 64. Further alternatively or additionally, standard image processing techniques, such as low pass filtering, are applied to the graph to prepare it for inspection by a physician.

Fig. 3C is a normalized graph of graph 64 of Fig. 3B designating the current sensed by probe 28 originating from anomaly 46, in accordance with an embodiment of the present invention.

The normalized graph is optionally displayed on a screen (not shown) to be analyzed by a physician searching for tumors which are suspected as being malignant. Conventionally,

the normalized graphs are displayed as a two dimensional map in which brighter shades signify areas in which high current levels were received while dark shades signify areas which received less current. Usually, most of breast 40 appears as an area with the same shade and anomalies stand out as much brighter areas.

As described above, in some embodiments of the invention, an imaging session includes a plurality of steps in which normalized maps of breast 40 are generated based on applied signals along different lines 36.

In some embodiments of the present invention, each of the normalized maps is displayed separately for inspection by the physician. Alternatively or additionally, the normalized maps are automatically analyzed separately using signal processing methods, by a processor associated with image head 12. The analysis optionally includes determining whether an anomaly exists in breast 40 and/or the location and depth of the anomaly. The results of the analysis are optionally displayed together with the respective maps, or in the form of a table summarizing substantially all the normalized maps. Alternatively or additionally, the analysis includes choosing (for display) one or more maps which best depict possible anomalies in breast 40. For example, the analysis may choose for displaying one or more maps in which the contrast between points within a small area is larger than a predetermined value.

It is noted that the current originating directly from elements 48 interfere with the detection of the current from anomaly 46. Generally, when more current is generated by probe 30 the detection of weak signals from anomalies far from probe 28 becomes harder. When elements 48 are electrified in a two-dimensional array, the strength of the signals substantially does not decrease with distance. When the elements are electrified in a one-dimensional array the signals decrease proportionally to the distance, and less interfere with the signals from anomaly 46. Therefore, it is desired to reduce the dimensionality of the applied signals. Furthermore, in many cases, signals from surface anomalies interfere with signals from a deep tumor which is to be detected. In such cases, the deep tumor is more readily identified when electrifying fewer elements 48 (Fig. 2).

For example, if a surface anomaly 52 is located on surface 42 it will form a dipole similar to the dipole formed in anomaly 46 which is to be detected. When a uniform electrical field is applied to probe 30 anomaly 46 and surface anomaly 52 form dipoles of substantially the same strength. On the other hand, the effect of anomalies 46 and 52 on sensors 34 is always dependent on the distance between the respective anomalies and sensors 34. Since the

dipole in surface anomaly 52 is closer to sensors 34 than anomaly 46, surface anomaly 52 has a stronger effect in the sensors than anomaly 46. By electrifying only a single line 36 on probe 30, the electric field within breast 40 decays proportionally to the distance from probe 30 and therefore the effect of anomaly 46 relative to surface anomaly 52 increases.

The dimensionality of the applied signals is reduced even more by using applied signals which interfere with each other, for example by electrifying two parallel lines 36 with opposite phases. The reduction of the dimensionality is especially important in the stage of determining the exact location of anomaly 46, especially the depth of the anomaly.

Fig. 4A is a schematic illustration of a first step of an imaging stage for determining the depth of anomaly 46, in accordance with an embodiment of the present invention. In some embodiments of the invention, after anomaly 46 is found, a dipole is induced within anomaly 46, as indicated by an arrow 78. The dipole in anomaly 46 induces within breast 40 an electrical field indicated by dashed lines 80. In some embodiments of the present invention, the dipole is induced by applying electrifying signals of different phases, e.g., opposite polarities, to a pair of lines 70 and 72 on opposite sides of the projection of the anomaly on probe 30, such that the center between lines 70 and 72 is located beneath the center of anomaly 46.

In some embodiments of the present invention, the depth determining stage begins with applying positive signals to line 70 without applying signals to line 72, i.e., applying negative signals of a zero amplitude. This electrification results in the dipole of anomaly 46 being pointed toward probe 28 (with a slight angle to the right which is negligible), as illustrated in Fig. 4A. The influence of the dipole induced within anomaly 46 on the array of sensors 34 is shown schematically by a graph 82. Graph 82 is a cross section of the normalized map formed by sensors 34 taken above anomaly 46. Graph 82 is optionally normalized using any of the normalization methods described above with relation to Figs. 3A-3C.

Graph 82 includes a single positive peak 84 above anomaly 46 and negative peaks 85 and 86 to the right and left of peak 84, respectively. The height of peak 84 depends on the location and characteristics of anomaly 46 similarly to peak 66 in Fig. 3B. For common anomalies, the height of peak 84 is about twice the background height (not shown, as the background was removed in the normalization). Designating the point above anomaly 46 as $x=0$, and the depth of anomaly 46 within breast 40, i.e., the distance between anomaly 46 and probe 28, as dp, peak 84 zeros approximately at $x=\pm\sqrt{2}$ dp, at which points negative peaks 85

and 86 begin. Peaks 85 and 86 have a maximal magnitude at about x=±2 dp from which points they substantially monotonously decay to -0 at infinity.

A negative signal of gradually increasing amplitude is optionally applied to line 72 while the amplitude on line 70 remains constant, resulting in the rotation of the dipole in anomaly 46.

Fig. 4B is a schematic illustration of an imaging step in which the dipole within anomaly 46 forms an angle relative to probes 28 and 30. Accordingly, field lines 80 also form an angle relative to probes 28 and 30. The influence of the dipole within anomaly 46 on the array of sensors 34 is shown schematically by a graph 82' in a manner similar to graph 82 of Fig. 4A. As the direction of the dipole indicated by arrow 78 tilts to the left, peaks 84, 85 and 86 move to the left, the magnitude of peak 85 on the right of peak 84 increases (i.e., becomes more negative), and the magnitude of peaks 84 and 86 decrease. Thus, the heights of peaks 84, 85 and 86 depend on the direction of the dipole within anomaly 46.

It is noted that peaks 84, 85 and 86 do not run along the entire length of probe 28 (into the page of Figs. 4A and 4B) but rather exist only around the position of anomaly 46.

The amplitude of the signals applied to the elements along line 72 is optionally increased until the direction of the dipole within anomaly 46, indicated by arrow 78 is substantially parallel to probe 30. Generally, the dipole within anomaly 46 is parallel to probe 30 when the amplitudes of the signals applied to lines 70 and 72 are substantially equal. It is noted, however, that this general rule may not be accurate, for example, due to inaccuracies in selection of lines 70 and 72. At this point, the distance between peaks 84 and 85 is optionally used to determine the depth dp of anomaly 46.

Fig. 4C is a schematic illustration of an imaging step in which the dipole within anomaly 46 is substantially parallel to probe 28. When the dipole within anomaly 46 is parallel to probe 28, peak 86 disappears and peaks 84 and 85 are of substantially equal magnitude, located anti-symmetrically around the point x=0 which is directly above anomaly 46. The distance d between peaks 84 and 85 is a function of the depth dp of anomaly 46 in breast 40, and of the size of anomaly 46. For anomalies of common sizes which are smaller than the depth dp, the distance d is substantially equal to depth dp. It is noted that for larger anomalies peaks 84 and 85 are smeared.

In some embodiments of the invention, the signals applied to lines 70 and 72 are interchanged and the above process is repeated. In some cases it is easier to detect positive peaks than negative peaks. Therefore, after detecting the precise location of one of peaks 84

and 85 the applied signals are reversed and the precise position of the other of the peaks is determined.

In some embodiments of the present invention, the process of determining the depth of anomaly 46 includes following the movements of peaks 84, 85 and 86. Detection of the peaks is easiest in the state shown in Fig. 4A, and the depth measurement is best performed in the state shown in Fig. 4C. Therefore, in some embodiments of the invention, the depth measurement is performed by gradually changing the signals applied to lines 70 and 72 and following the changes in peaks 84 and 85 until the peaks are of the same size. In some embodiments of the invention, the movements of peaks 84 and 85 are induced automatically by a controller which controls the signals applied to lines 70 and 72. Optionally, the controller also determines when peaks 84 and 85 are of equal size. Alternatively or additionally, the determination when peaks 84 and 85 have equal sizes and/or the inducing of the movements of peaks 84 and 85 are performed under manual control oh a physician.

Alternatively or additionally to moving peaks 84, 85 and 86 by gradually changing the direction of the dipole within anomaly 46, the peaks may be moved by other methods, such as by moving the electrification lines 70 and/or 72 along probe 30. In this alternative, lines 70 and 72 with a constant distance between them are optionally passed along probe 30 until peaks 84 and 85 have equal sizes. In some embodiments of the present invention, lines 70 and 72 are passed over probe 30 while having equal amplitudes and substantially opposite polarities, thus forming a dipole between the lines. The dipole formed by lines 70 and 72 induces an electrical field within breast 40, which field induces a counter dipole within anomaly 46, as indicated by arrow 78.

In this alternative, the direction of the dipole within anomaly 46 is a function of the distance between anomaly 46 and lines 70 and 72. When lines 70 and 72 are far from the projection of anomaly 46 on probe 30, the direction of the dipole within anomaly 46 is substantially from probe 30 to probe 28, as shown in Fig. 4A. As the dipole formed of lines 70 and 72 approaches the projection of anomaly 46, the dipole within anomaly 46 rotates until it becomes parallel to probe 30 when the projection of anomaly 46 is substantially between lines 70 and 72.

It is noted that since the electrical field induced by lines 70 and 72 is regular in the dimension parallel to lines 70 and 72, the influence of the field on probe 28 is canceled in the normalizing of the map. Therefore, only the influence due to the dipole within anomaly 46 appears on the maps generated by probe 28. It is also noted that the current due to direct

influence from lines 70 and 72 declines proportionally to the square of the distance and therefore interferes to a lesser extent in determining the current from anomaly 46 than current from a single positive line 36 as described above with reference to Fig. 2.

In some embodiments of the present invention, the location of the projection of anomaly 46 on probe 28 is determined, as described above, using the method of Fig. 2 and/or a method in which substantially all the elements of probe 30 are electrified. Alternatively or additionally, the location of the projection of anomaly 46 is determined by electrifying lines 70 and 72 sequentially along probe 30 with a fixed distance between the lines, and finding the positions of lines 70 and 72 for which peaks 84 and 85 have the same magnitude and/or for which peak 86 disappears. Optionally, breast 40 is scanned a few times with different distances between lines 70 and 72. In some embodiments of the present invention, relatively large distances between lines 70 and 72 are used, in order to enhance the strength of the dipole within anomaly 46. The average point between peaks 84 and 85 is substantially directly above anomaly 46. After the location of the projection of anomaly 46 on probe 28 is determined the depth of anomaly 46 is optionally determined using the method of Figs. 4A-4C. Thus, the three coordinates of anomaly 46 are determined using a sensing probe 28 which covers only a single side of breast 40, or stated otherwise, covers less than 50%, even 25%, of the total surface area of breast 40.

In another embodiment of the present invention, a first detection stage is performed in which substantially all the elements 48 of probe 30 are electrified. Those areas which show irregularity are scanned using a single line 36, as described with reference to Fig. 2, in a second stage. In a third stage, those anomalies detected in the second stage are examined using pairs of lines with opposite polarity in order to determine the depths of the anomalies. In some embodiments of the invention, the depth is determined from both probes 28 and 30, by alternately using one of the probes for providing electrifying signals and the other one of the probes for sensing the signals.

In some embodiments of the present invention, a plurality of maps for different electrification patterns are prepared concurrently by applying the electrification signals of the different patterns simultaneously, using different frequencies. For example, signals at different frequencies may be applied concurrently to lines 70 or to pairs of lines 70 and 72 concurrently thus scanning the entire region in one or a few electrifying steps. Optionally, the frequencies used are within a relatively narrow band, such that the impedance measure does not differ significantly between the frequencies. For example, frequencies between 1000Hz and 1600Hz

at steps of 20Hz may be used to form over 30 maps concurrently. In another example, frequencies between 200 kHz and 500 kHz with steps of 10 kHz, or frequencies between 300-330KHz with steps of 1KHz, are used.

In some embodiments of the present invention, the estimated depth of anomalies is superimposed on the representation of the anomaly on a map of the breast. Alternatively or additionally, the physician may point (e.g., using a mouse) at an area on the map and responsive thereto the processor displays information on the pointed area including, for example, an approximated depth, and/or a size and shape of an anomaly at the pointed area.

In some embodiments of the present invention, the processor provides the physician with information extracted from a plurality of the normalized maps. In some embodiments of the invention, the physician is provided with an output which includes the percentage of maps in which an anomaly was detected. Optionally, the location and depth of the anomaly are determined as a weighted average of the location and depth from all the maps in which it was detected. Optionally, maps generated with applied signals closer to anomaly 46 are given more weight in the weighted average.

Alternatively or additionally, the location and depth of anomaly 46 are determined directly from the normalized graphs of a plurality of steps. Further alternatively or additionally, a superposition graph of some or all of the graphs from different steps is displayed. Alternatively or additionally, only graphs which are determined to be interesting, i.e., are substantially different from expected graphs for healthy breasts, are displayed for examination by the physician.

In some embodiments of the invention, the normalized map displayed to the physician responsive to the method of Figs. 4A-4C is corrected so as to indicate the point above anomaly 46 instead of peaks 85 and 86. Optionally, peaks 85 and 86 are replaced by a single peak at the center point between peaks 85 and 86. The replacement peak is optionally given a height which is a weighted average of the absolute heights of peaks 85 and 86. Alternatively, the height of the replacement peak is a function of the depth of anomaly 46. Further alternatively, the height of the replacement peak is a predetermined arbitrary value which makes the anomaly appear clearly on the normalized map.

In some embodiments of the invention, sensors 34 are kept at a virtual ground level, or at any other equipotential level, which attracts electrical currents from probe 30 towards probe 28. In this embodiment, sensors 34 optionally have a low input impedance. Thus, probe 28 affects the electrical signals being measured. Specifically, only currents perpendicular to probe

28 can exist in the proximity of probe 28 and generally it is easier to detect dipoles which are perpendicular to probe 28 than dipoles which are parallel to probe 28.

Alternatively or additionally, sensors 34 measure the electric signals in a manner which minimizes their influence on the fields. In some embodiments of the present invention, some or all of sensors 34 are connected with a high input impedance. In this embodiment, an electrode separate from probes 28 and 30 (not shown) is optionally attached to breast 40 or to another surface of the patient's body in order to attract the currents applied by probe 30. Optionally, each point on an impedance map receives a value based on the difference between the signals sensed by two adjacent sensors 34. In some embodiments of the invention, sensors 34 are very close to each other, e.g., of a difference of a centimeter or less, such that their measurements are substantially at the same point.

In another embodiment of the invention, sensors 34 are operated in a low impedance mode but are turned on sequentially rather than concurrently, such that at any single time only a small fraction of sensors 34 influence the field within breast 40. Thus, the field within breast 40 is not forced to be perpendicular to probe 28. It is noted that detecting dipoles which are parallel to probe 28 is much easier when sensors 34 substantially do not influence the field within breast 40.

In some embodiments of the invention, most of sensors 34 sense voltages while a small fraction of the sensors sense currents and attract the currents from probe 30. In this embodiment the signals are sensed in a single step without the need of an external electrode to attract the currents. Possibly, the low impedance sensors are located in the center of probe 30, for example, along a line parallel to lines 70 and 72 or in a central circle or square.

In some embodiments of the present invention, some of sensors 34 have a high input impedance while others have a low input impedance. Thus, in some steps the sensing may be performed with the high input impedance sensors and in other steps the sensing is performed with the low input impedance sensors.

Fig. 5 is a schematic illustration of a sensor 54, in accordance with an embodiment of the present invention. Sensor 54 has a controllable input impedance which is changed for different sensing steps as required. Sensor 54 optionally receives input signals from a pair of contacts 56 which contact human surfaces in a manner similar to sensors 34. In some embodiments of the invention, contacts 56 are part of an array of contacts similar to probes 28 and 30. In some embodiments of the invention, a first pair of switches 55 connects contacts 56 to a ground potential. A second pair of switches 57 connects contacts 56 to a voltage

measurement amplifier 58 which measures the voltage differential between the contacts 56. In some embodiments of the invention, voltage measurement amplifier 58 has a high input impedance as is known in the art. In some embodiments of the invention, voltage measurement amplifier 58 comprises an INA unit, for example, the INA2128 available from Burr Brown.

A third pair of switches 59 optionally connect contacts 56 to current measurement circuits 49, which measure the currents on contacts 56 separately. Current measurement circuits 49 optionally comprise an operational amplifier 47, such as the AD746 available from Analog Devices. Optionally, circuit 49 comprises an impedance circuit 51 parallel to the operational amplifier 47. In some embodiments of the invention, impedance circuit 51 comprises a resistor of about 100 kohm and a capacitor of about 47pF in parallel. The outputs from voltage measurement amplifier 58 and current measurement circuits 49 are optionally passed through a selector 53 to an analog to digital converter 61.

During their operation, each of contacts 56 is optionally in one of four states set by switches 55, 57 and 59. In a first state, contact 56 is connected to amplifier 58 for voltage measurement. In some embodiments of the invention, in this state, both of contacts 56 are connected to amplifier 58. In a second state, contact 56 is connected to current measurement circuit 49. In a third state contact 56 is connected to a ground potential in order to generate an equipotential surface while other contacts 56 are measuring currents (or voltages). In a fourth state, contact 56 is left floating (unconnected) preventing the contact 56 from influence measurements performed by other contacts 56.

In some embodiments of the invention, the high impedance input of amplifier 58 is substantially higher than the impedance levels within breast 40. The low impedance input of circuit 49 is optionally substantially lower than the impedance levels within breast 40.

After the position of the anomaly is determined, non-invasive diagnostic methods are optionally used in order to determine the nature of anomaly 46. In some embodiments of the invention, signals of various frequencies and amplitudes are applied beneath the determined area at which anomaly 46 was found in order to generate a diagnostic impedance image of the vicinity of anomaly 46, as described, for example, in above mentioned US patent 5,810,742.

In some embodiments of the present invention, a plurality of diagnostic images of different frequencies are produced simultaneously, using the method described above. Optionally, the frequencies used in creating the diagnostic images are as close as possible to frequencies which are suitable for physiological considerations while allowing creation of the diagnostic images using a single FFT operation. Alternatively or additionally, the frequencies

used in creating the diagnostic images are dispersed evenly on a logarithmic scale of a band of useful frequencies.

In some embodiments of the present invention, a predetermined number of beginning frequencies are selected throughout the useful spectrum (between a few Hz and a few MHz), optionally according to physiological considerations of the tissue of the scanned region. Thereafter, the beginning frequencies are optionally adjusted such that each frequency has a different "alias" in the Nyquist regime, i.e., each frequency occupies a different "bin" in the Fourier spectrum. Optionally, the adjusting begins with the lower frequencies by bringing the lower frequencies to the nearest bins and continues with the higher frequencies which are brought to the nearest of the remaining bins. This is because adjustments in high frequencies are less significant than in low frequencies. The selecting of frequencies with different aliases in the Nyquist regime allows using the FFT operation in creating impedance maps from the sensed signals. Alternatively or additionally, at least some of the frequencies are selected without relation to the Nyquist regime and algebraic operations are used in constructing impedance maps.

In some embodiments of the present invention, an entire examination session is performed automatically by a processor, based on preprogrammed instructions to probes 30 and 28. The processor optionally determines which elements of probe 30 are electrified in each step and which elements of probe 28 sense the signals, and how. In addition, the processor optionally normalizes the maps sensed by probes 28 and calculates the depth of suspected anomalies, as described above. In some embodiments of the invention, the processor also determines whether additional tests are required responsive to results of earlier tests in the session and optionally automatically performs these additional tests. For example, when a suspected dark point of a borderline size is detected, the processor initiates additional tests to determine whether the dark point represents an anomaly which requires a biopsy test. Thus, the physician does not need to intervene with the operation of image head 12.

Alternatively or additionally, the physician manually instructs a controller of image head 12 which imaging steps and/or stages are to be performed and/or sets parameters of the steps and/or stages, such as the distance between lines 70 and 72. Further alternatively or additionally, the physician controls each step of the examination session, including the identities of the elements 48 electrified in each step.

Although the above description refers to a specific embodiment of probes 28 and 30, many other probes may be used to carry sensors 34 and/or to apply the electrifying signals. For

example, elements 48 may be mounted on various types of flexible probes. In some embodiments of the present invention, elements 48 are mounted on probes suitable for insertion into the body of a patient so as to apply the electrifying signals and/or sense the resultant signals as close as possible to a suspected tumor. For example, elements 48 may be mounted on a fingertip probe, on a laparoscopic probe, and/or on an intra-operative paddle type probe, as described in the above referenced U.S. patent 5,810,742. In some embodiments of the present invention, elements 48 are mounted on an invasive tool, such as a biopsy needle, to help lead the tool toward a tumor, as described hereinbelow.

Fig. 6 is a schematic illustration of an impedance imaging system 90, in accordance with an embodiment of the present invention. System 90 comprises a hand held sensing probe 92 and a pair of electrifying probes 94, which are optionally firmly attached to opposite sides of breast 40. The use of a hand held probe 92 for sensing allows a physician to control the position of sensing probe 92 and choose the best location for examining a specific area of breast 40. Furthermore, when the physician desires to insert a biopsy needle or other invasive tool to breast 40, sensing probe 92 is easily moved by the physician to make room for the insertion of the needle.

Electrifying signals are applied to probes 94 in order to induce a dipole within an anomaly 46 located within breast 40. Optionally, electrifying probes 94 operate as current sources of the same magnitudes with opposite phases such that currents flow within breast 40 from one of probes 94 to the other. In some embodiments of the invention, each probe 94 comprises a single element such that the probe applies the same signals from its entire surface. Alternatively, probes 94 comprise arrays of elements in any of the arrangements described with reference to probe 30.

Probe 92 optionally comprises a two dimensional array of sensors as described above with reference to probe 30. In some embodiments of the present invention, the sensors of sensing probe 92 measure the electric signals in a manner which minimizes the influence of sensing probe 92 on the measured signals. The induced currents, therefore, flow primarily between probes 94, inducing a dipole within anomaly 46, and only minimally influencing the measurements of sensing probe 92. Thus, the signals from anomaly 46 are easily detected by sensing probe 92 since the signals are not obscured by the currents flowing between probes 94. Furthermore, the dipole within anomaly 46 is substantially parallel to sensing probe 92 allowing determination of the depth of anomaly 46 within breast 40, as described hereinabove.

The sensed signals from probe 92 are optionally normalized in any of the methods described above and the resulting images are optionally displayed to the physician on a screen (not shown). It is noted, however, that since the signals sensed by probe 92 are primarily from anomaly 46 it is possible to display the signals sensed by probe 92 after a primitive normalization or without any normalization for a partially degraded map.

Fig. 7 is a schematic illustration of a method of leading an impedance guided needle 100 toward a tumor 46 within a breast 40, in accordance with an embodiment of the present invention. In the embodiment of Fig. 7, needle 100 generates electrifying signals so that the position of the needle relative to tumor 46 is easily viewed by a physician. Impedance guided needle 100 comprises a biopsy needle, or any other invasive tool, which is formed, at least partially, of a conducting material.

Electrical signals are optionally applied to needle 100 while it is inserted to breast 40. A probe 28 situated on an external side of breast 40 optionally senses the electrical signals reaching the surface of the breast. The signals from needle 100 appear on probe 28 in the form of a wedge-shaped line along the projection of the needle onto probe 28. The depth of needle 100 beneath probe 28 is related to the width of the wedge-shaped line, and in most practical applications can be assumed to be proportional to the width. This is because the farther needle 100 is from probe 28 the more the current from the needle disperses. In some embodiments of the invention, a processor determines the width of the wedge-shaped line at the edges of needle 100 and accordingly determines the depth orientation of the needle within breast 40. The other orientations of needle 100 are determined from the projection of the needle on probe 28.

In addition to allowing the detection of the position and orientation of needle 100 within breast 40, currents from needle 100 generally flow through anomaly 46 because of the low impedance of the anomaly. As needle 100 approaches anomaly 46 the strength of the signals from anomaly 46 intensify, providing an additional indication of the location of the tip of needle 100 relative to anomaly 46. When needle 100 contacts anomaly 46, the tumor becomes substantially an electrical extension of needle 100, in a manner largely increasing the surface signals from anomaly 46, detected by probe 28.

In general, the signals applied to needle 100 induce a dipole within anomaly 46. The direction of the dipole within anomaly 46 depends on the relative orientation between needle 100 and anomaly 46. If needle 100 approaches anomaly 46 from the opposite side of probe 28, the dipole in anomaly 46 is directed toward probe 28 and is best detected by low input impedance sensors. If, on the other hand, needle 100 approaches anomaly 46 in an orientation

perpendicular to probe 28, the dipole within the anomaly is perpendicular to probe 28. Therefore, the sensors on probe 28 are optionally given a high input impedance.

In some embodiments of the present invention, in addition to electrifying needle 100, an external probe 108 applies signals to a surface of breast 40, optionally substantially opposite probe 28. Probe 108 is optionally similar to any of the embodiments of probe 30 described above although other probes may be used as well.

In some embodiments of the present invention, probe 28 is held at an equipotential level and probe 108 applies voltage signals. The potential difference between probes 28 and 108 falls substantially equally over breast 40, since the impedance of the tissue of breast 40 is substantially constant. The electrifying signals applied to needle 100 are optionally voltage signals which are frequency and phase correlated with the signals from probe 108. Since needle 100 comprises a conducting material the signals applied to needle 100 are the same over the entire length of the needle. The voltage of breast 40 surrounding needle 100, on the other hand, depends on the distance of needle 100 from probes 108 and 28. In an example, based on DC voltages for simplicity, probe 28 is held at 0V and probe 108 is held at 2V. The central layer 110 between probes 28 and 108 is therefore at about 1V. If needle 100 is held at 1V, those parts of the needle which are above layer 110, closer to probe 28, are at voltage levels higher than their surrounding. Therefore, those parts of needle 100 give out currents to their surroundings, and appear on the screen as a line brighter than their surroundings. On the other hand, those parts of needle 100 which are below layer 110, closer to probe 108, appear on the screen darker than their surroundings.

In some embodiments of the present invention, the voltage at which needle 100 is held is gradually changed until part of the needle appears darker than its surroundings and part of the needle appears lighter than its surroundings. At this state the voltage applied to needle 100 is equal to the voltage of the surroundings of the needle in at least one point. Based on this voltage, the depth of various portions of the needle within breast 40 can be estimated.

Alternatively or additionally, the voltage at which needle 100 is held is gradually changed until part of the needle disappears from the screen, joining the surroundings of the needle. This alternative is especially useful when needle 100 is substantially parallel to probe 28 and/or probe 108.

In some embodiments of the invention, needle 100 and probe 108 apply signals of opposite polarity. Thus, a dipole is formed between needle 100 and surface probe 108, inducing a dipole within anomaly 46. When needle 100 forms contact with (or is very close to)

anomaly 46, the polarity of the dipole reverses providing additional indication that needle 100 is in place.

Alternatively or additionally, the signals are applied to needle 100 and surface probe 108 at separate instances so that they do not interfere with each other. In some embodiments of the present invention, signals are substantially constantly applied to surface probe 108 to receive a general map of a vicinity of needle 100. Periodically and/or when otherwise appropriate signals are applied to needle 100 in order to precisely determine the location of the needle.

Further alternatively or additionally, signals at one or more first frequencies are applied to surface probe 108 in order to detect the position of anomaly 46. Signals at one or more second frequencies are optionally applied to needle 100 so that it is possible to detect the position of the needle. In some embodiments of the present invention, signals at one or more third frequencies are applied to both needle 100 and probe 108 in order to induce a dipole within anomaly 46 as described above. Optionally, the first, second and third frequencies are within a narrow band over which the impedance measure does not change significantly.

In some embodiments of the present invention, at a first stage, signals are applied only to surface probe 108 in order to detect the location of anomaly 46 using any of the methods described above. These signals are optionally continuously applied in order to keep constant track of the detected anomaly 46. When needle 100 is directed to anomaly 46, signals are also applied to the needle to keep track of the movements of the needle and/or determine the relative position between the anomaly and the needle.

Fig. 8 shows a biopsy needle 112, in accordance with an embodiment of the invention, which is used to improve the accuracy of placement of the needle. Biopsy needle 112 includes a plurality of sensing elements 104 placed around the circumference of the needle, such that they indicate which portion of the needle is within a tumor to be biopsied. Alternatively or additionally, sensing elements 104 are spaced along the length of the needle. Leads (not shown) from each of these elements bring signals from the elements to a detection and computing system such as that described below. Alternatively, the electrodes may be circumferentially segmented (a lead being provided for each segment) so that information as to the direction of the tumor from the needle may be derived when the needle is not within the tumor.

Such an impedance sensing biopsy needle can be used, under guidance by palpation, ultrasound, x-ray mammography or other image from other image modalities (optionally

including impedance imaging as described herein), taken during the biopsy or prior to the biopsy to improve the accuracy of placement of the needle. In particular, the impedance image from the needle may be combined with other images in a display. While this aspect of the invention has been described using a biopsy needle, this aspect of the invention is also applicable to positioning of any elongate object such as any other needle (such as a localizing needle), an endoscopic probe or a catheter.

In some embodiments of the present invention, electrical signals are applied from probes 108 and/or 28 (Fig. 7) and the resultant signals are sensed by elements 104. In some embodiments of the present invention, the readings on the different elements 104 are compared to determine which of elements 104 are in contact with anomaly 46. In some embodiments of the invention, in which circumferentially segmented sensing elements are employed, the direction of the anomaly 46 relative to needle 112 is determined from the sensed signals. Alternatively or additionally, the sensed signals are used to determine the proximity of needle 112 to anomaly 46.

The image sensing biopsy needle can also be used with one or more imaging arrays (similar to those in probes 28 and 30) to impedance image the region to be biopsied during the biopsy procedure. Alternatively, at least one of the arrays can be an imaging array of the non-impedance type.

In some embodiments of the present invention, one or more of the elements on the needle may themselves be electrified to cause them to "light up" on the image of probes 28 and/or 108. This electrification may be AC or DC may be the same or different from the primary image stimulus, may have a single frequency or a complex form and may be applied in a continuous or pulsed mode. In some embodiments of the invention, elements 104 are electrified at various phases, for example at opposite polarities to provide electrification in the form of a dipole.

If one or more of the sensing elements is used in this manner for applying electrifying signals, the elements are optionally alternatively used to apply an electrification signal and to function as sensors, i.e., to sense signals from the primary stimulus.

In some embodiments of the present invention, electrifying elements 104 face different directions of advancement. Optionally, when there is a doubt on the orientation of the needle, electrifying signals are applied sequentially to elements 104 and the orientation is determined accordingly, for example, according to the element 104 which induced the largest surface signals in probe 28.

It is noted that in a single biopsy procedure, elements 104 may serve both for applying electrical signals and for sensing signals. Alternatively or additionally, some of elements 104 serve as sensors and some apply signals, simultaneously.

In some embodiments of the present invention, needle 112 includes, in addition to elements 104, a position sensor (not shown) of any kind known in the art which is used to locate the needle in a manner independent of the applied electrical signals. In some embodiments of the present invention, the position sensor keeps track of the position of needle 112 even when electrical signals are not applied from elements 104. Optionally, after the position of needle 112 is determined relative to anomaly 46 using impedance imaging, the position of the needle in the impedance framework is registered with the position sensor framework, and the needle is tracked using the position sensor. Thus, it is possible to stop electrifying elements 104, for example in order not to interfere with precisely determining the position of anomaly 46.

It will be appreciated that the above described methods may be varied in many ways, including, changing the order of steps, and the exact implementation used. It should also be appreciated that the above described description of methods and apparatus are to be interpreted as including apparatus for carrying out the methods and methods of using the apparatus.

The present invention has been described using non-limiting detailed descriptions of embodiments thereof that are provided by way of example and are not intended to limit the scope of the invention. It should be understood that features described with respect to one embodiment may be used with other embodiments and that not all embodiments of the invention have all of the features shown in a particular figure. Variations of embodiments described will readily occur to persons of the art. Furthermore, the terms "comprise," "include," "have" and their conjugates, shall mean, when used in the claims, "including but not necessarily limited to." The scope of the invention is limited only by the following claims:

CLAIMS

1. Apparatus for impedance imaging of a region within a subject, comprising:

a plurality of electrodes adapted to, substantially concurrently, apply electrical signals having a common frequency and different phases to the subject; and

a plurality of sensing elements adapted to sense electrical signals from a surface of the region, responsive to signals applied from the electrodes.

2. Apparatus according to claim 1, wherein the plurality of sensing elements are included in a multi-element probe including a two-dimensional array of sensing elements.

3. Apparatus according to claim 2, comprising a screen for displaying an image of the region responsive to signals sensed by the sensing element.

4. Apparatus according to claim 3, wherein the screen is adapted to display an image which represents a projection of the region on to the multi-element probe.

5. Apparatus according to any of claims 2-4, comprising a sensing controller adapted to initiate sensing by at least one of the sensing elements while at least one of the sensing elements is kept electrically floating.

6. Apparatus according to any of the preceding claims, wherein the plurality of electrodes are adapted to apply signals with opposite phases to the subject.

7. Apparatus according to any of the preceding claims, wherein the plurality of electrodes are adapted to apply signals with equal amplitudes to the subject.

8. Apparatus according to any of the preceding claims, wherein the plurality of electrodes are adapted to apply signals with frequencies above 40KHz to the subject.

9. Apparatus according to any of the preceding claims, wherein the plurality of electrodes are adapted to apply signals in the form of at least one dipole to the subject.

10. Apparatus according to any of the preceding claims, wherein the plurality of electrodes are adapted to apply signals in the form of at least one long and narrow line to the subject.

11. Apparatus according to any of the preceding claims, comprising a processing unit adapted to determine a depth of an anomaly beneath the sensing elements responsive to the sensed signals.

12. Apparatus according to claim 11, wherein the processing unit is adapted to determine a distance between peaks on a map of the sensed signals.

13. Apparatus according to any of the preceding claims, wherein the plurality of electrodes are included in an electrode probe and wherein the apparatus includes a controller adapted to electrify less than all the electrodes of the electrode probe.

14. Apparatus according to any of the preceding claims, wherein at least one of the plurality of sensing elements has a high input impedance.

15. Apparatus for impedance imaging of a region within a subject, comprising:

a multi-element probe comprising a plurality of electrifyable elements adapted to apply electrical signals to the region;

an electrification controller adapted to electrify a group including at least one long and narrow line of the electrifyable elements of the probe, but less than all the electrifyable elements; and

a plurality of sensing elements adapted to sense electrical signals from the region, responsive to signals applied by the electrodes.

16. Apparatus according to claim 15, wherein the probe comprises a two-dimensional array of electrifyable elements and the electrification controller is adapted to electrify at least one column or row of the elements of the probe.

17. Apparatus according to claim 15 or 16, wherein the electrification controller is adapted to sequentially apply electrical signals to lines of elements of the multi-element probe.

18. Apparatus according to any of claims 15-17, wherein the electrification controller is adapted to electrify concurrently at least two rows or lines of the elements of the multi-element probe.

19. Apparatus according to claim 18, wherein the electrification controller is adapted to apply electrical signals to parallel pairs of lines of elements of the multi-element probe.

20. Apparatus according to claim 18 or 19, wherein the electrification controller electrifies concurrently at least two rows or lines of the probe, with signals having different amplitudes, frequencies or phases.

21. Apparatus according to any of claims 15-20, wherein the plurality of sensing elements are included in a multi-element probe including a two-dimensional array of sensing elements.

22. Apparatus according to any of claims 15-21, wherein at least some of the sensing elements are held at an equipotential level.

23. Apparatus according to any of claims 15-22, comprising an analysis unit which analyses the region responsive to signals sensed by the sensing elements.

24. Apparatus according to claim 23, wherein the analysis unit analyses the region also responsive to the positions of the electrodes applying the electrical signals.

25. Apparatus according to claim 23 or 24, wherein the analysis unit determines at least one characteristic of an anomaly within the region.

26. Apparatus according to claim 25, wherein the analysis unit determines a depth of an anomaly within the region.

27. Apparatus according to claim 25 or 26, wherein the electrification controller is capable of determining a medical diagnosis of the anomaly.

28. Apparatus according to any of claims 23-27, wherein the analysis unit is capable of determining whether an anomaly exits in the region.

29. Apparatus according to any of claims 15-28, wherein the multi-element probe is mounted on an invasive tool adapted to be inserted into the region.

30. Apparatus according to any of claims 15-29, wherein the plurality of sensing elements are mounted on an invasive tool adapted to be inserted into the region.

31. Apparatus according to any of claims 15-30, wherein the electrification controller generates a current tracing map responsive to the measured signals.

32. Apparatus according to claim 31, wherein the electrification controller normalizes the current tracing map.

33. Apparatus according to claim 32, wherein the electrification controller normalizes the map by subtracting background values from the generated map.

34. Apparatus according to claim 32 or 33, wherein the electrification controller normalizes the map by subtracting, from the measured signals of at least one group of elements, a representative value of the group.

35. Apparatus according to any of claims 15-34, wherein the plurality of electrifyable elements are adapted to apply signals at frequencies above 40 kHz.

36. Apparatus for impedance imaging of a region, comprising:

an electrifying probe which applies a plurality of distinct electrifying signals to the region; and

a sensing probe, comprising a two dimensional array of sensing elements which sense signals generated responsive to the plurality of distinct electrifying signals.

37. Apparatus according to claim 36, wherein the plurality of distinct electrifying signals are of substantially the same frequency.

38. Apparatus according to claim 36 or 37, wherein the plurality of distinct electrifying signals are of substantially the same amplitude.

39. Apparatus according to any of claims 36-38, wherein the plurality of distinct electrifying signals have different phases.

40. Apparatus for impedance imaging of a region, comprising:

at least one first electrode adapted to apply currents to the region;

at least one second electrode adapted to attract currents from the region;

a probe, comprising a plurality of sensing elements for sensing signals induced by the applied currents; and

circuitry which is adapted to measure signals from a plurality of the sensing elements and generate an impedance map based on the differences between the measurements of pairs of adjacent sensing elements.

41. Apparatus according to claim 40, wherein the at least one second electrode and the at least one first electrode are adapted to be positioned on opposite sides of the region.

42. Apparatus according to claim 40 or 41, wherein the probe comprises at least one sensing element having a high input impedance.

43. Apparatus according to claim 42, wherein the probe comprises at least one sensing element having a low input impedance.

44. Apparatus according to any of claims 40-43, wherein the probe comprises at least one sensing element having a controllable input impedance.

45. Apparatus according to any of claims 40-44, wherein the probe comprises at least one pair of sensing elements which are separated by less than a centimeter.

46. Apparatus for sensing electrical signals from a tissue surface, comprising:

at least one contact surface suitable for contact with the tissue surface; and

a sensing circuit with a controllable input impedance, which senses electrical signals incident on the at least one contact surface.

47. Apparatus according to claim 46, wherein the sensing circuit comprises one or more switches which select one of a plurality of predetermined input impedance values.

48. Apparatus according to claim 46 or 47, wherein the input impedance of the sensing circuit may be set to a substantially zero input impedance.

49. Apparatus according to any of claims 44-48, wherein the input impedance of the sensing circuit may be set to a substantially infinite input impedance.

50. Apparatus according to any of claims 44-49, wherein the at least one contact surface comprises at least one sharp edge which penetrates an upper layer of the tissue surface.

51. Apparatus according to any of claims 46-49, wherein the at least one contact surface comprises a flat surface.

52. Apparatus for sensing electrical signals from a tissue surface, comprising:

a two dimensional array of sensing elements, at least one of the sensing elements has a high input impedance; and

circuitry which generates an impedance map responsive to signals sensed by the sensing elements.

53. Apparatus according to claim 52, wherein substantially all the sensing elements have a high input impedance.

54. Apparatus according to claim 52 or 53, wherein the at least one sensing element with a high input impedance comprises at least one sharp edge which penetrates an upper layer of the tissue surface.

55. Apparatus for impedance imaging of a region within a subject, comprising:

at least one electrifyable element capable of electrifying the subject;

a multi-element probe, comprising a plurality of sensing elements, capable of measuring signals from the region;

circuitry capable of generating a map from the signals sensed by the sensing elements; and

a processing unit adapted to determine a depth of an anomaly beneath the multi-element probe responsive to the generated map.

56. Apparatus according to claim 55, wherein the at least one electrifyable element is adapted to apply electrical signals with different phases to the subject.

57. Apparatus according to claim 55 or 56, wherein the processing unit determines a distance between two peaks on the map.

58. Apparatus according to any of claims 55-57, wherein the processing unit is adapted to determine a point on the map above the anomaly, responsive to the generated map.

59. Apparatus for determining a location of an elongate object in a region of a subject, comprising:

at least one surface probe adapted to induce an electrical condition in the region;

a multi-element probe adapted to sense electrical signals from a surface of the region;

circuitry adapted to generate an impedance map responsive to signals sensed by the multi-element probe;

a power source adapted to apply electrical signals to the elongate object; and

a controller adapted to adjust at least one parameter of the electrical signals provided to the elongate object, such that the location of the elongate object in the region may be determined responsive to an imprint of signals from the elongate object on the impedance map.

60. Apparatus according to claim 59, wherein the controller automatically adjusts the at least one parameter responsive to the impedance map.

61. Apparatus according to claim 59 or 60, wherein the controller provides an indication when the location of the elongate object in the region may be determined responsive to the imprint of signals from the elongate object on the impedance map.

62. Apparatus according to claim 61, wherein the controller provides an indication when the imprint of the elongate object on the map has a lower amplitude than surrounding signals at a first portion of the map and a higher amplitude than surrounding signals at a second portion of the map.

63. Apparatus according to any of claims 59-62, wherein the controller is adapted to determine a depth of the elongate object responsive to the signals applied to the elongate object.

64. Apparatus for impedance imaging of a region within a subject, comprising:

an electrification probe adapted to apply electrifying signals at a plurality of distinct frequencies to the region through different respective electrifying elements;

a sensing probe, comprising a plurality of sensing elements, adapted to sense signals from a surface of the region responsive to electrifying signals applied to the region by the electrification probe; and

circuitry adapted to create a plurality of maps for the distinct frequencies responsive to signals sensed by the sensing elements.

65. Apparatus according to claim 64, wherein the sensing probe is adapted to sense signals a predetermined number of times during a sensing period and wherein the number of distinct frequencies comprises substantially the maximal number allowed by the predetermined number of samplings according to Nyquist's law.

66. Apparatus according to claim 64 or 65, wherein the circuitry generates the plurality of maps using a single FFT operation.

67. A method of impedance imaging of a region within a subject, comprising:

positioning a first multi-element probe, comprising a plurality of sensing elements, on one side of the region;

positioning a second multi-element probe including a plurality of electrifyable elements on a second side of the region;

electrifying at least one of the plurality of electrifyable elements forming a long and narrow line, but less than all the electrifyable elements; and

measuring a signal at at least some of the sensing elements.

68. A method according to claim 67, comprising sequentially electrifying and measuring while electrifying different sub-groups of elements of the second multi-element probe.

69. A method according to claim 68, wherein sequentially electrifying comprises sequentially electrifying pairs of one-dimensional strips of the second multi-element probe.

70. A method according to claim 69, wherein sequentially electrifying the pairs of one-dimensional strips comprises electrifying the one-dimensional strips with signals of respective opposite polarities.

71. A method according to claim 69 or 70, wherein electrifying the pairs of one-dimensional strips comprises electrifying pairs of one-dimensional strips which are separated by a predetermined distance, to form a dipole source of electrification.

72. A method according to any of claims 67-71, comprising analyzing the region responsive to the measured signals and the positions of the electrified elements.

73. A method according to any of claims 67-72, wherein the electrified elements cover an area which is less than ten percent of a face area of the multi-element probe.

74. A method according to any of claims 67-73, wherein positioning the electrifyable elements comprises mounting the electrifyable elements on an invasive tool inserted into the region.

75. A method according to any of claims 67-74, wherein electrifying the electrifyable elements comprises applying at least two electrifying signals with different phases.

76. A method according to claim 75, wherein applying the at least two electrifying signals comprises applying signals of substantially opposite polarity.

77. A method according to any of claims 67-76, wherein positioning the multi-element probe comprises holding substantially all of the sensing elements of the first multi-element probe at a same potential.

78. A method of impedance imaging of a region, comprising:

positioning a multi-element probe, comprising a plurality of sensing elements, on a surface of the region;

providing an electrifying field to the region substantially in the form of a dipole; and

measuring a signal at at least some of the elements of the multi-element probe responsive to the electrifying field.

79. A method according to claim 78, wherein providing the dipole electrifying field comprises providing signals of opposite polarity to spaced electrifyable elements.

80. A method according to claim 78 or 79, wherein providing the electrifying field comprises providing the field from a dipole formed of parallel lines.

81. A method of impedance imaging of a region, comprising:

positioning a multi-element probe, comprising a plurality of sensing elements, on a surface of the region;

providing a plurality of electrifying fields of different phases to the region; and

measuring a signal at at least some of the elements of the multi-element probe responsive to the electrifying fields.

82. A method according to claim 81, wherein providing the plurality of electrifying fields comprises providing fields which comprise a dipole field.

83. A method according to claim 81 or 82, wherein providing the plurality of electrifying signals comprises providing signals which have voltages such that the sum of the voltages of the signals is substantially zero at substantially any time.

84. A method of impedance imaging of a region, comprising:

positioning a multi-element probe, comprising a plurality of sensing elements, on a surface of the region;

applying an electrical field to the region;

connecting at least some of the sensing elements of the multi-element probe to a sensor through a high input impedance;

measuring an electrical signal produced by at least some of the sensing elements with the high input impedance sensor; and

producing an impedance map responsive to the difference between the measured signals of pairs of at least some of the sensing elements.

85. A method according to claim 84, wherein applying the electrical field comprises applying signals to a pair of electrodes on substantially opposite sides of the region.

86. A method according to claim 85, wherein applying the signals to the pair of electrodes comprises applying signals to a pair of electrodes positioned such that a straight line connecting the electrodes is substantially parallel to the multi-element probe.

87. A method according to claim 85 or 86, wherein applying the signals to the pair of electrodes comprises applying signals to a pair of electrodes positioned substantially perpendicular to the multi-element probe.

88. A method according to any of claims 85-87, wherein applying the signals to the pair of electrodes comprises applying signals to a pair of electrodes such that the combined field produced by electrification of the pair of electrodes is substantially parallel to the multi-element probe.

89. A method according to any of claims 85-88, wherein applying the signals comprises applying signals of a different amplitude to each of the electrodes.

90. A method according to claim 89, wherein applying the signals to the pair of electrodes comprises holding one of the electrodes at a ground potential.

91. A method of impedance imaging of a region, comprising:

positioning a multi-element probe, comprising a plurality of adjacent sensing elements, on a surface of the region;

positioning a pair of electrodes on substantially opposite sides of the region;

electrifying the pair of electrodes to provide an electrical field between the pair of electrodes;

measuring an electrical signal by at least some of the sensing elements responsive to the electrifying of the pair of electrodes; and

producing an impedance map of the region responsive to the difference between the signals measured by adjacent sensing elements.

92. A method of determining the position of an anomaly within a region of a body, comprising:

applying electrifying signals to the region;

determining a response map along a surface of the region responsive to the applied signals;

determining a point on the surface which is above the anomaly responsive to the response map; and

calculating a depth from the determined point to the anomaly responsive to the response map.

93. A method according to claim 92, wherein determining the response map comprises determining a map which covers less than half the total surface area of the region.

94. A method according to claim 92 or 93, wherein determining the response map comprises determining a plurality of maps generated responsive to different patterns of electrifying signals.

95. A method according to any of claims 92-94, wherein determining the point above the anomaly comprises finding a point located between a pair of peaks on the map.

96. A method according to claim 95, wherein calculating the depth comprises determining a distance between the pair of peaks.

97. A method according to any of claims 92-96, wherein applying electrifying signals to the region comprises inducing a dipole which is substantially parallel to the surface along which the response map is determined.

98. A method of impedance imaging of a region, comprising:

positioning a probe, comprising a plurality of sensing elements, on a surface of the region;

simultaneously applying electrifying signals at a plurality of distinct frequencies to the region through different electrifying elements; and

measuring electrical signals by at least some of the sensing elements responsive to the applied electrifying signals.

99. A method according to claim 98, comprising determining a separate influence on the region, of the signals of at least one of the distinct frequencies responsive to the measured signals.

100. A method according to claim 98 or 99, wherein measuring the electrical signals comprises sampling signals by the sensing elements a predetermined number of times and wherein the number of distinct frequencies comprises substantially the maximal number allowed by the predetermined number of samplings according to Nyquist's law.

101. A method according to any of claims 98-100, comprising selecting a plurality of beginning frequencies and adjusting the frequencies so as to fit into nearest vacant Nyquist bins in order to receive the distinct frequencies.

102. A method according to claim 101, wherein selecting the plurality of beginning frequencies comprises selecting based on physiological characteristics of the region.

103. A method according to claim 102, wherein adjusting the frequencies comprises adjusting low frequencies before high frequencies.

104. A method according to any of claims 98-103, wherein applying electrifying signals at a plurality of distinct frequencies comprises applying signals at frequencies only within a narrow band in which impedance measures do not change substantially.

105. A method according to any of claims 98-104, wherein simultaneously applying electrifying signals at a plurality of distinct frequencies comprises placing an electrification probe including an array of electrodes on a surface of the region and electrifying different electrodes of the array with different frequencies.

106. A method according to any of claims 98-105, comprising generating separate maps for a plurality of the distinct frequencies responsive to the measured electrical signals.

107. A method according to claim 106, wherein generating the separate maps is performed using a single FFT operation.

108. A method according to claim 107, wherein the distinct frequencies are selected so as to allow generating the separate maps using the single FFT operation.

109. A method according to any of claims 106-108, wherein generating the separate maps is performed using algebraic operations.

110. A method of guiding an elongate object within a region of a subject, comprising:

providing electrifying signals to at least a part of the elongate object within the region;

providing electrifying signals, different from the signals provided to the at least a part of the elongate object, from a surface of the region;

measuring electrical signals on a surface of the region;

moving the elongate object;

comparing the electrical signals measured on the surface of the region before and after the movement; and

determining desired movements of the object responsive to the comparison.

111. A method according to claim 110, wherein providing the electrifying signals from the surface comprises providing signals of opposite polarity of the signals provided to the elongate object.

112. A method according to claim 110 or 111, wherein the elongate object comprises a biopsy needle.

113. A method according to any of claims 110-112, wherein providing the electrifying signals comprises providing the signals to a probe mounted on the elongate object.

114. A method according to any of claims 110-112, wherein providing the electrifying signals comprises electrifying the elongate object.

115. A method according to any of claims 110-113, wherein determining the desired movements comprises determining a movement direction which enhances the measured signals.

116. A method for determining the location of an elongate object in a region of a subject, comprising:

providing electrifying signals to at least a part of the elongate object within the region;

measuring electrical signals on a surface of the region; and

providing an indication responsive to a reversal of the polarity of the measured signals.

117. A method for determining the location of an elongate object in a region of a subject, comprising:

providing electrifying signals to at least a part of the elongate object within the region;

measuring electrical signals on a surface of the region; and

determining a depth of a plurality of points along the elongate object, relative to the surface from which the signals are measured, responsive to the measured signals.

118. A method according to claim 117, wherein measuring the electrical signals comprises producing a two dimensional map of signals on the surface of the region.

119. A method according to claim 118, wherein determining the location of the object comprises determining a depth of the object responsive to the width of an image of the object on the two dimensional map.

120. A method according to claim 118 or 119, wherein determining the location of the object comprises determining a depth of the object responsive to the strength of the signals on the two dimensional map.

121. A method according to any of claims 118-120, further comprising providing electrifying signals to the region from a surface of the region.

122. A method according to claim 121, comprising varying the amplitude of the signals provided to the at least part of the elongate object.

123. A method according to claim 122, wherein determining the location of the object comprises generating a two dimensional map responsive to the measured signals and determining an amplitude of the electrifying signals provided to the object at which at least part of an image of the object on the map is not distinguishable from its surroundings.

124. A method according to claim 122, wherein determining the location of the object comprises generating a two dimensional map responsive to the measured signals and determining an amplitude of the electrifying signals provided to the object at which at least part of an image of the object is darker than its surroundings on the map and at least part of the image of the object is brighter than its surroundings on the map.

125. A method for determining a location of an elongate object in a region of a subject, comprising:

providing electrifying signals to a part of the elongate object within the region;

measuring electrical signals on a surface of the region;

generating a map of the region responsive to the measured signals; and

changing the electrical signals provided to the elongate object so that the surface signals generated responsive to the signals provided to the elongate object are lower than

surrounding surface signals on the map at a first portion of the map and higher than surrounding surface signals on the map at a second portion of the map.

126. A method according to claim 125, wherein changing the electrical signals comprises changing an amplitude of the signals.

127. A method according to claim 126, wherein determining the location of the object comprises determining a depth of the object responsive to the amplitude of the changed signals.

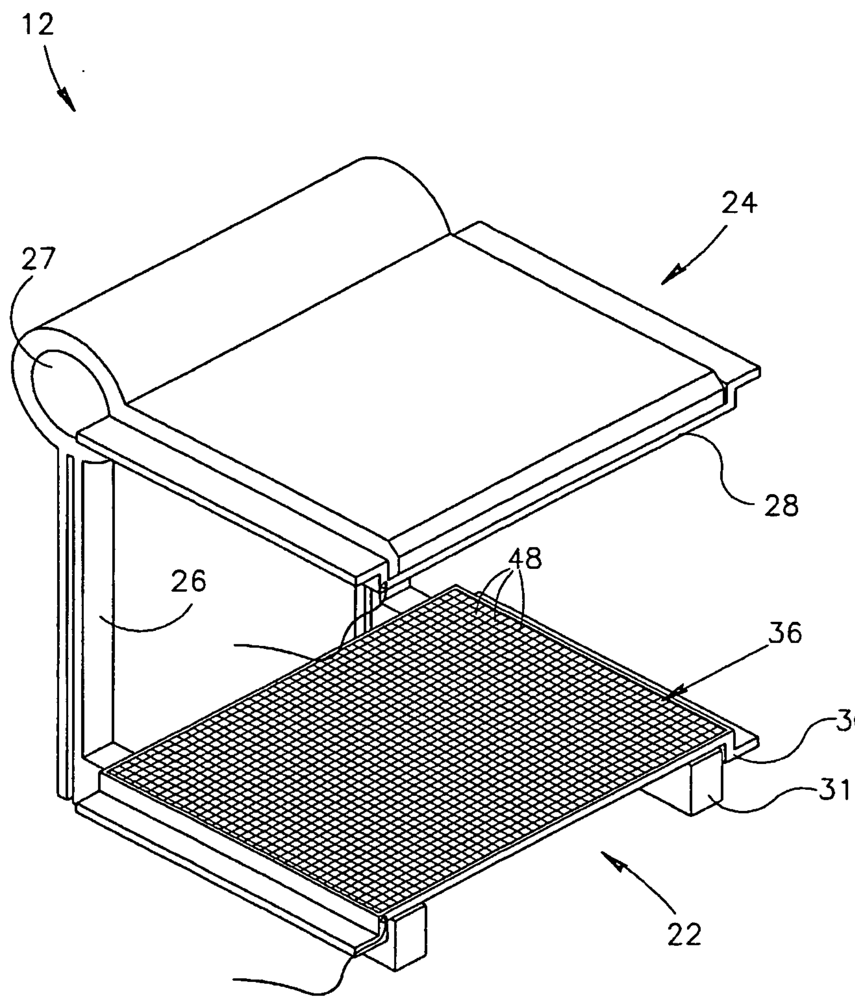


FIG.1

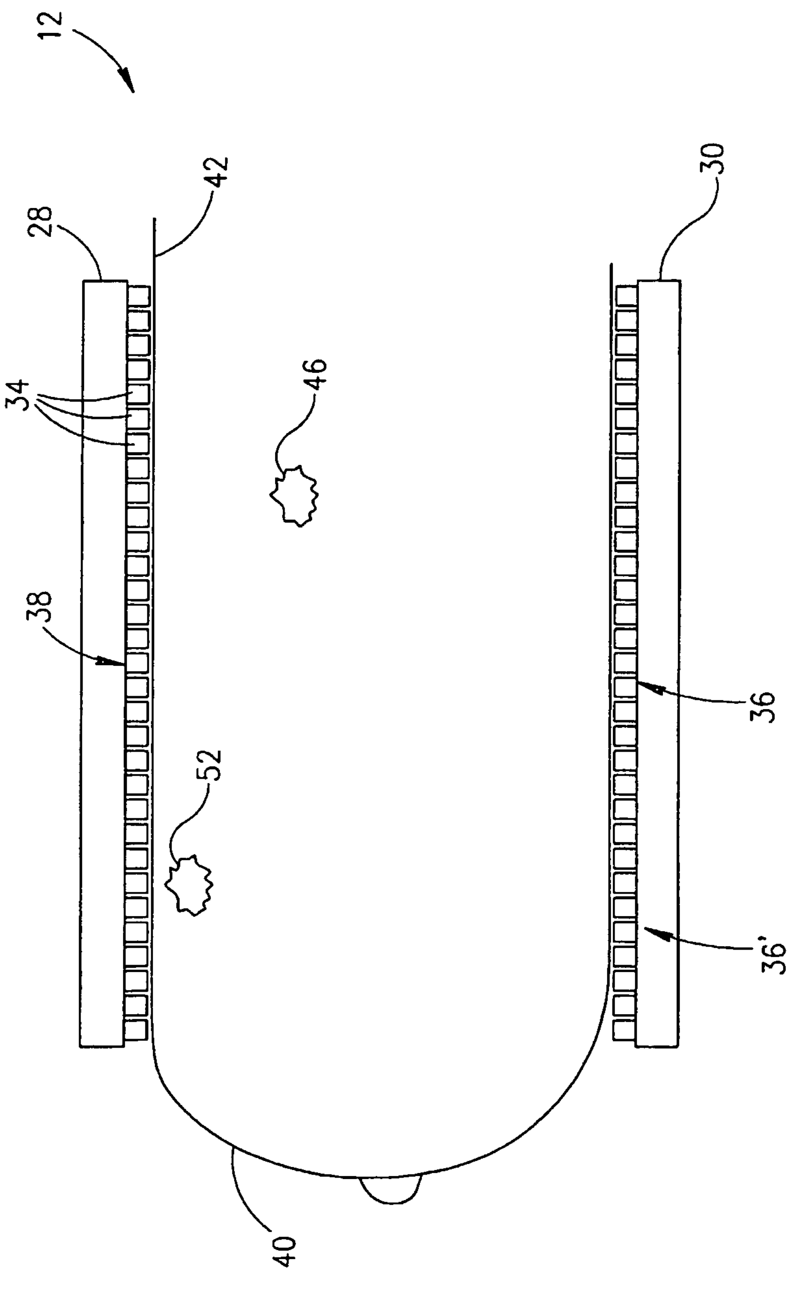


FIG.2

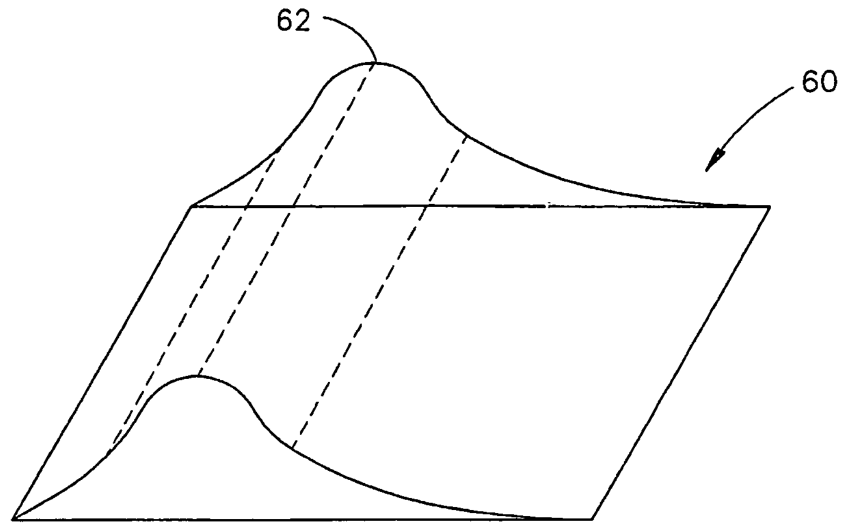


FIG.3A

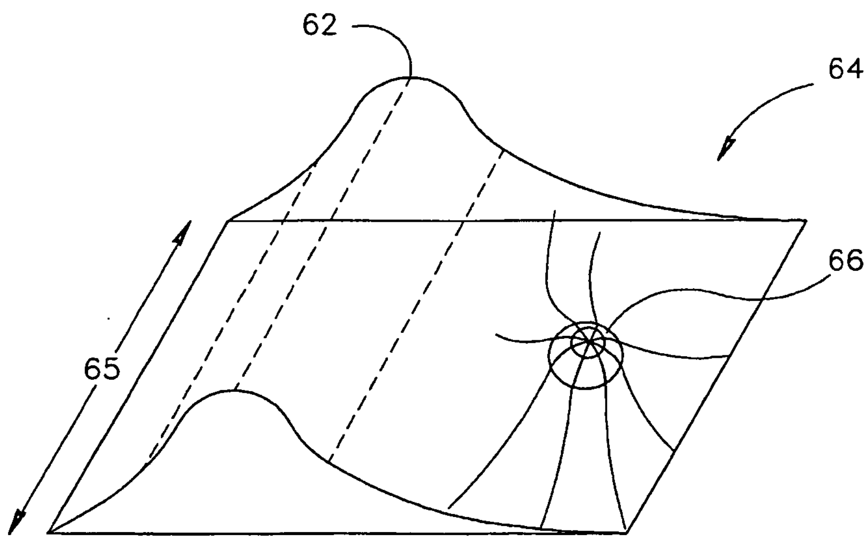


FIG.3B

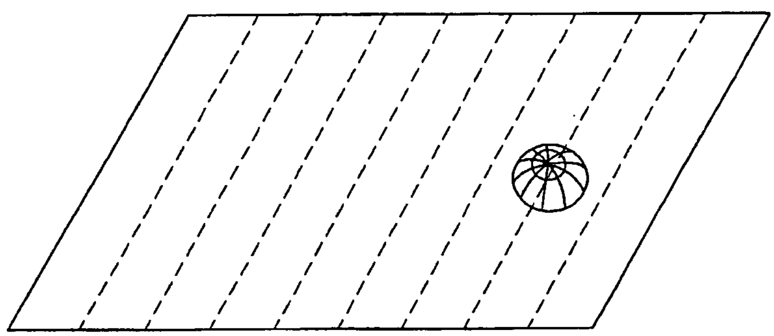


FIG.3C

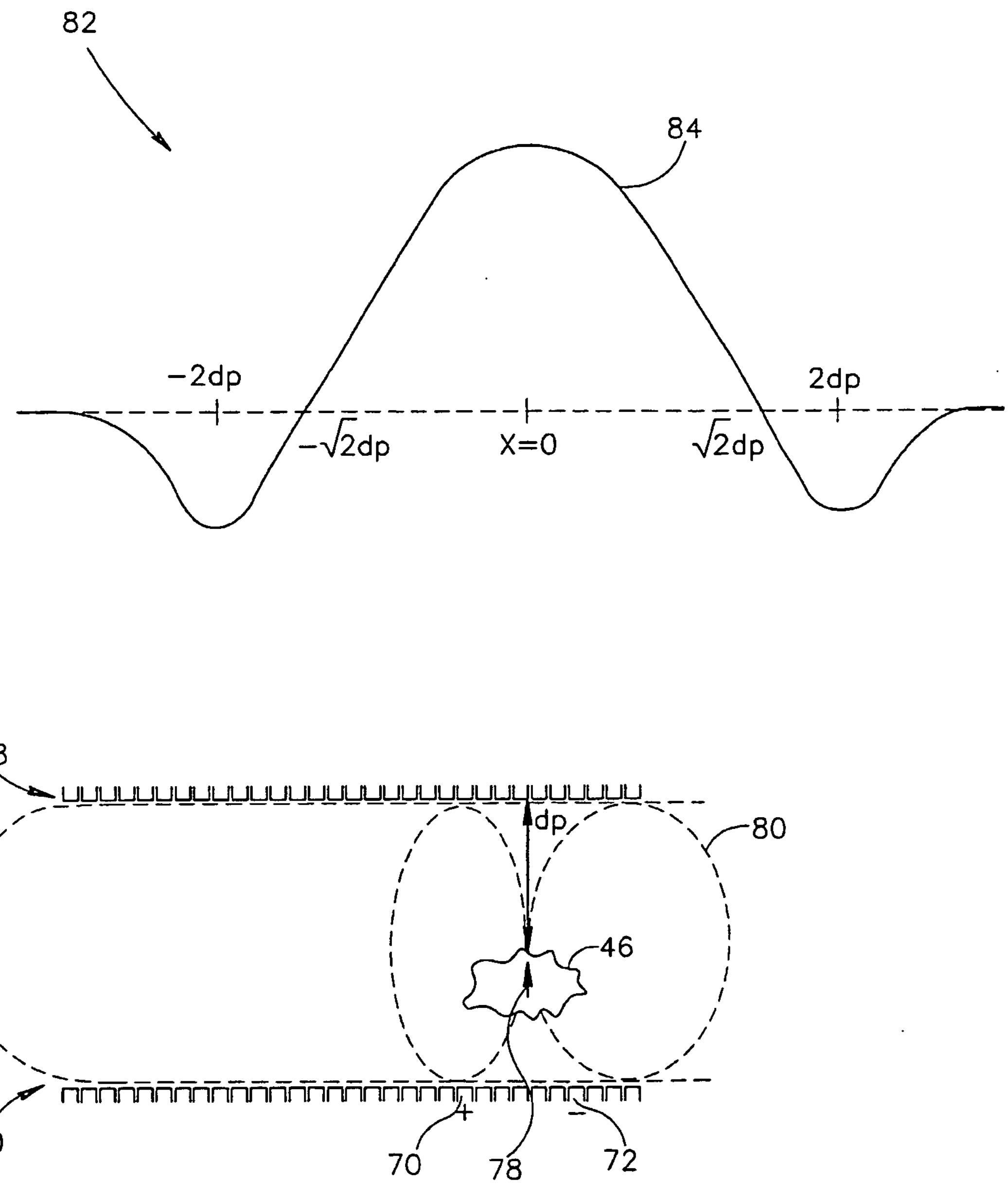


FIG.4A

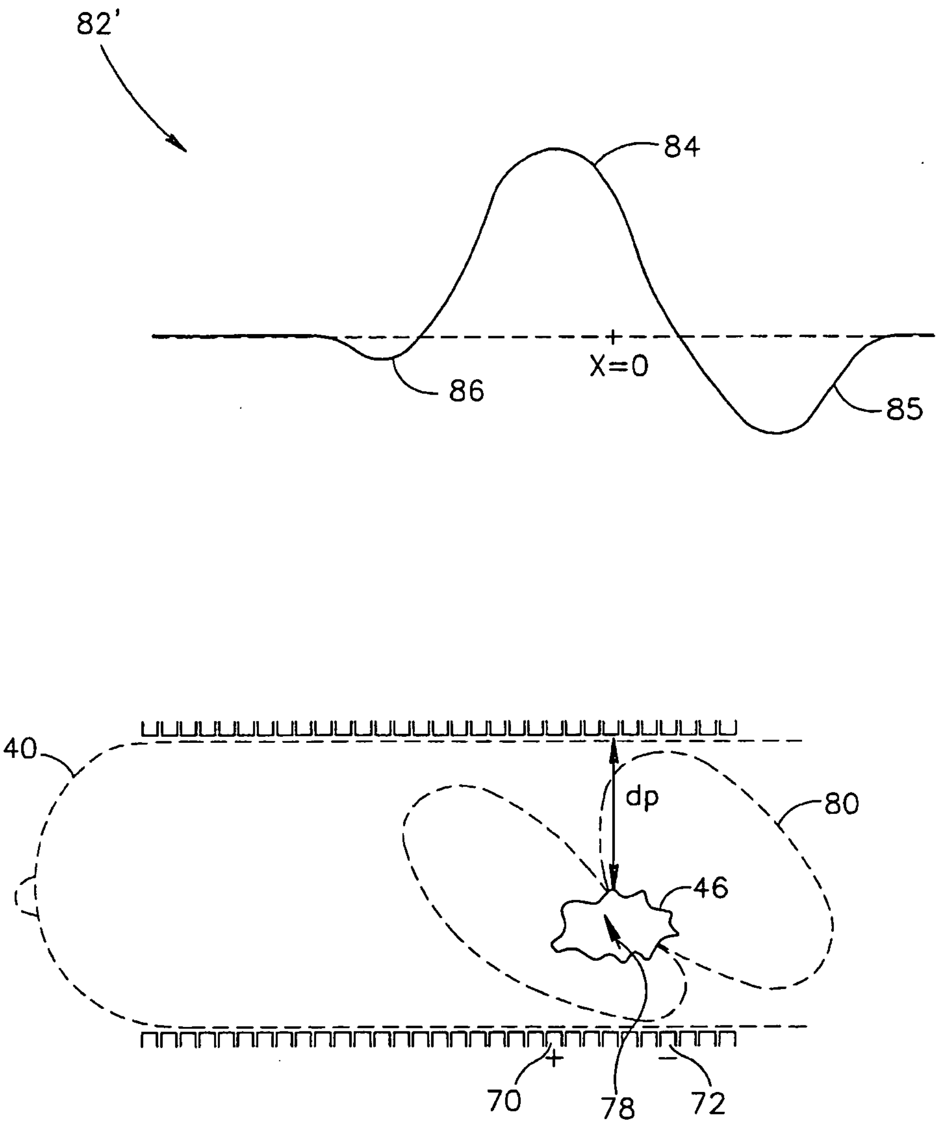


FIG.4B

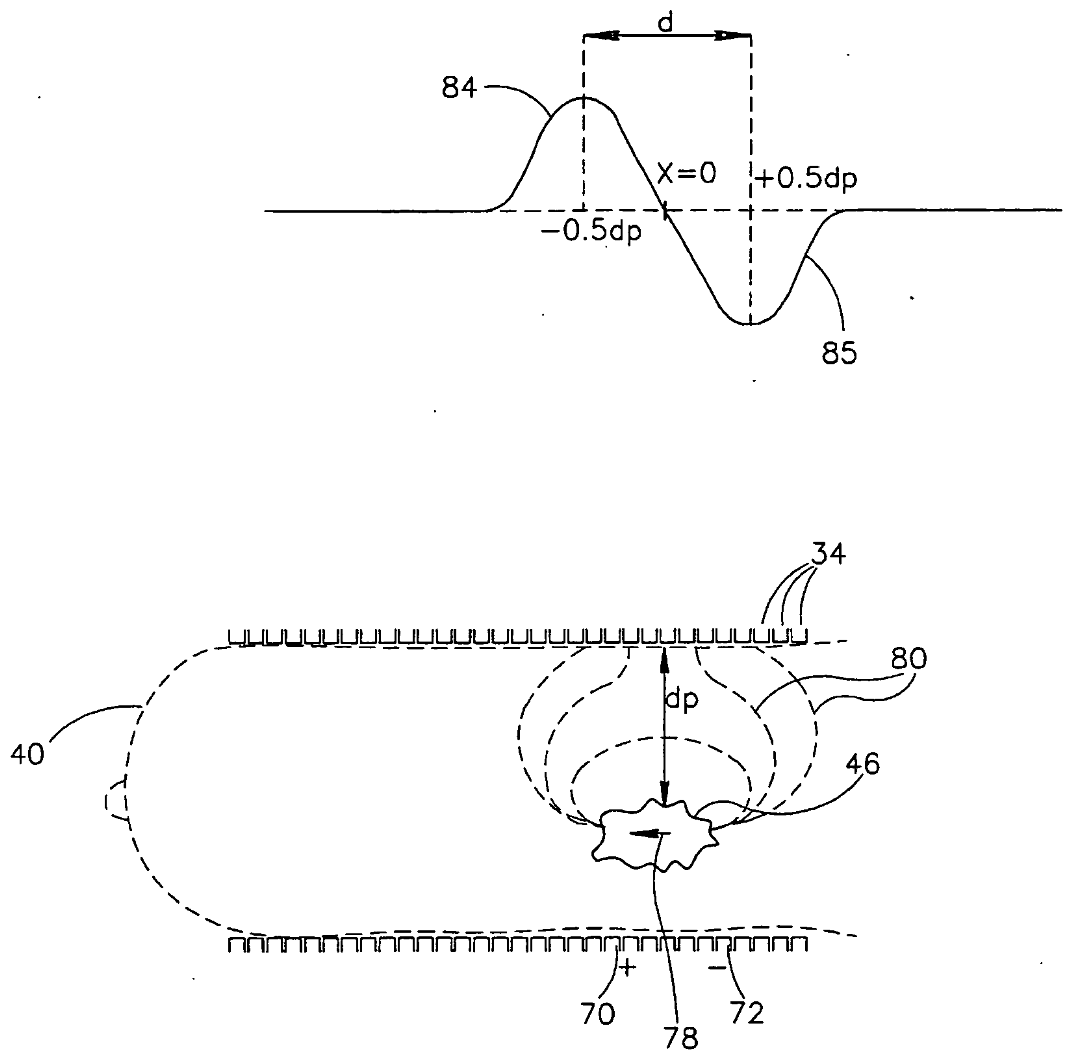
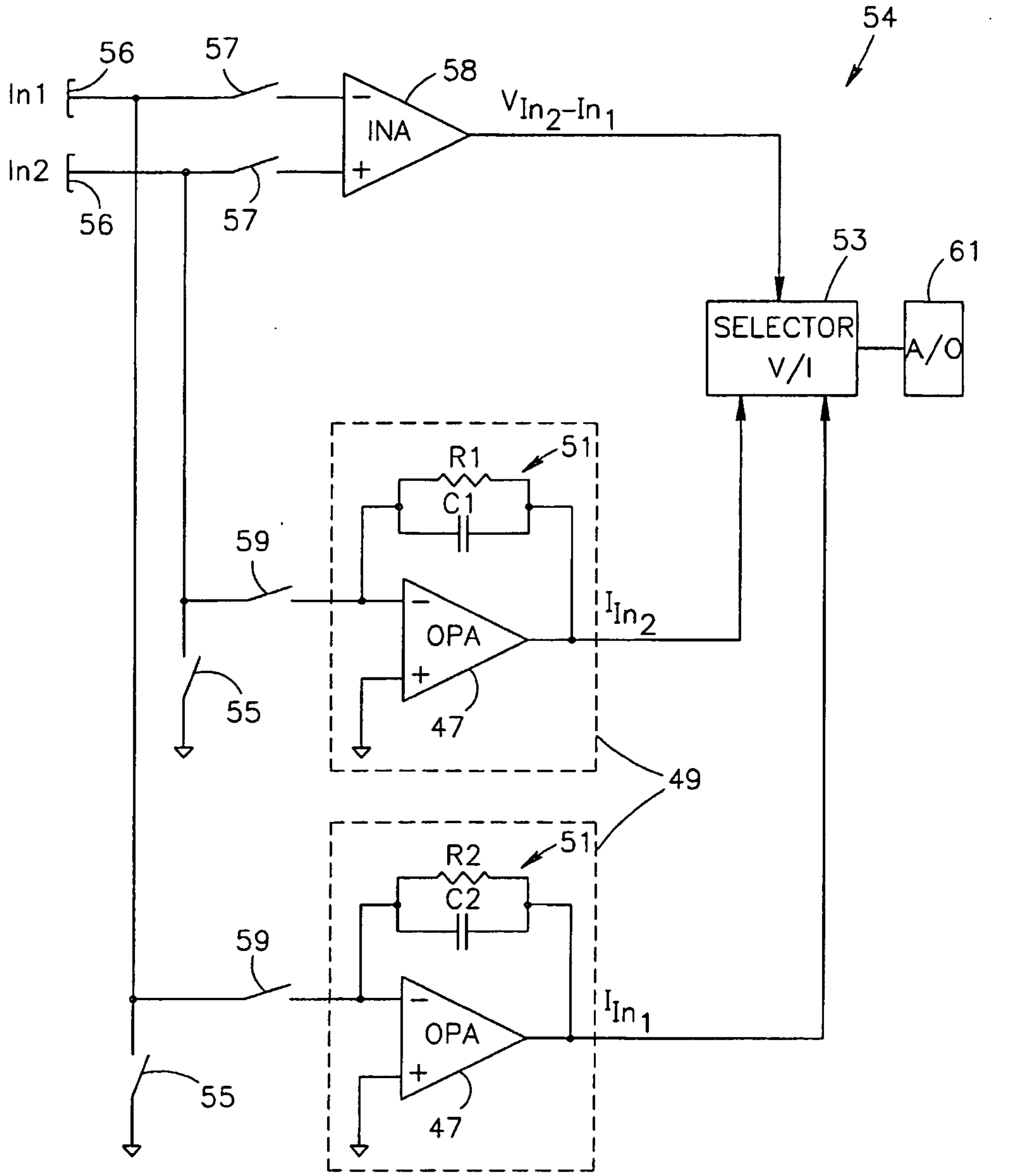


FIG.4C


54
In1
56
57
58
INA
$V_{In_2-In_1}$
In2
56
57
53
61
SELECTOR
V/I
A/O
R1
51
C1
59
OPA
I_{In_2}
55
47
49
R2
51
C2
59
OPA
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55
47

FIG.5

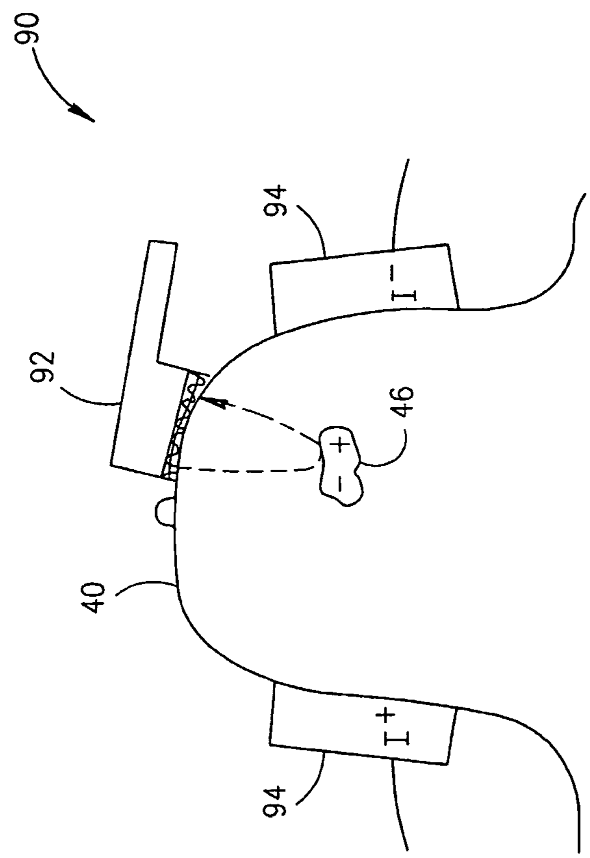

FIG.6

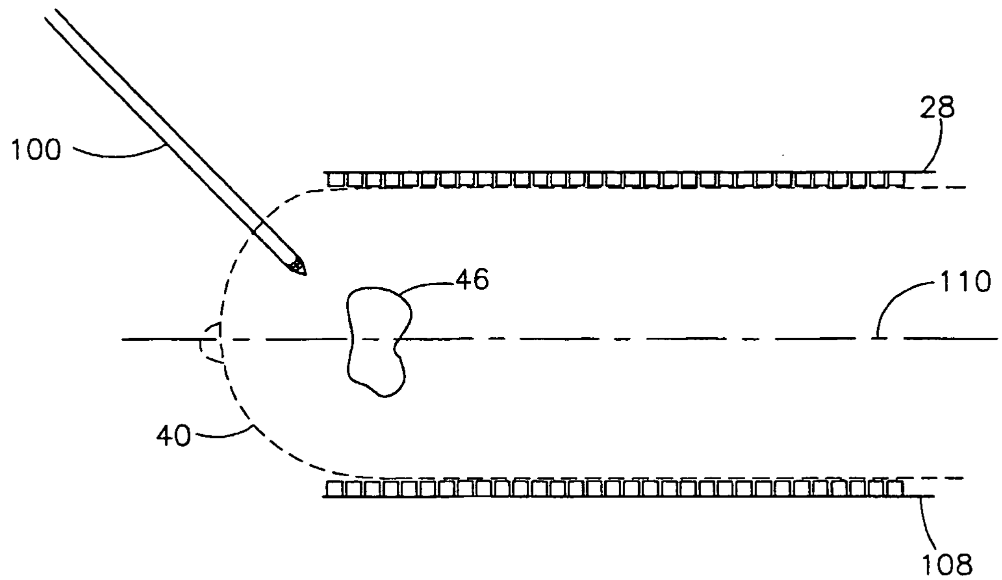

FIG.7

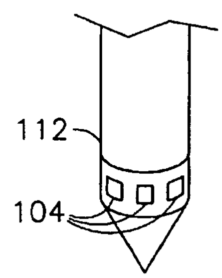

FIG.8